CHAPTER 9

Glaucoma

Introduction

Physiology of aqueous production

The ciliary body consists of the anterior pars plicata (2 mm wide) and the posterior pars plana (4 mm wide). The pars plicata bears 70 radially orientated ciliary processes which project into the posterior chamber. Each ciliary process is lined by a pigmented epithelial layer continuous with the retinal pigment epithelium and a non-pigmented epithelial layer continuous with the neuroretina. Each process also has a central arteriole ending in a rich capillary network. Tight junctions between adjacent non-pigmented epithelial cells constitute the blood–aqueous barrier. Aqueous humour is actively secreted by the non-pigmented epithelium as a result of a metabolic process that depends on several enzyme systems, especially the Na^+/K^+-ATPase pump, which secretes Na^+ ions into the posterior chamber. Water follows passively along the osmotic gradient. Carbonic anhydrase also plays a role, but the precise mechanism is uncertain. Aqueous secretion is diminished by factors that inhibit active metabolism such as hypoxia and hypothermia but it is independent of the level of intraocular pressure (IOP). Analysis of the hydrostatic and osmotic pressures across the ciliary epithelium reveals that under normal conditions passive secretion plays little, if any, role in the genesis of aqueous humour. Aqueous secretion is diminished by the following:

- Drugs such as beta-blockers, sympathomimetics and carbonic anhydrase inhibitors.
- Cyclodestructive procedures such as cyclocryotherapy and laser ablation.
- Ciliary body shutdown which may be caused by: detachment of the ciliary body, inflammation of the secretory ciliary epithelium associated with iridocyclitis and retinal detachment.



Fig. 9.1
Scanning electron microgram of the trabecular meshwork

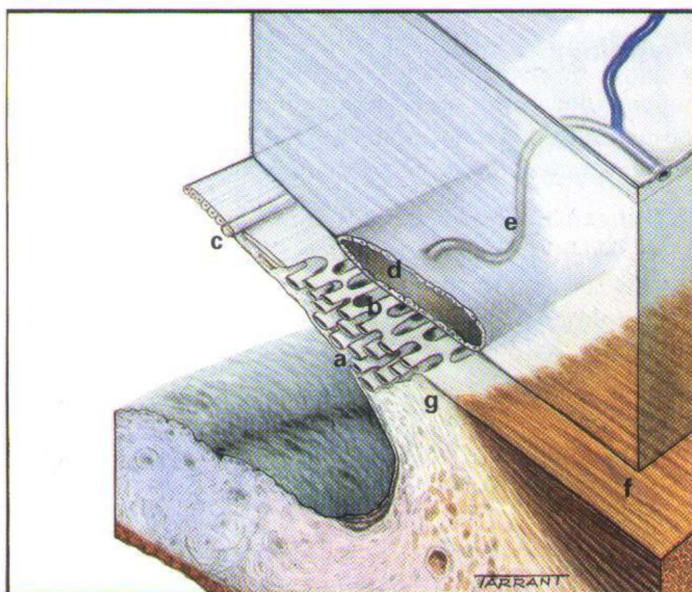


Fig. 9.2
Anatomy of the outflow channels. **(a)** Uveal meshwork; **(b)** corneoscleral meshwork; **(c)** Schwalbe line; **(d)** Schlemm canal; **(e)** collector channels; **(f)** longitudinal muscle of the ciliary body; **(g)** scleral spur

Aqueous outflow

Anatomy

1. **The trabecular meshwork** (trabeculum) is a sieve-like structure at the angle of the anterior chamber, through which 90% of the aqueous humour leaves the eye (Fig. 9.1). It consists of the following three portions:
   a. ***The uveal meshwork*** (Fig. 9.2a) is the innermost portion, which consists of cord-like meshes that extend from the root of the iris to Schwalbe line (Fig. 9.2c). The intertrabecular spaces are relatively large and offer little resistance to the passage of aqueous.
   b. ***The corneoscleral meshwork*** (Fig. 9.2b) forms the larger middle portion which extends from the scleral spur (Fig. 9.2g) to Schwalbe line. The meshes are sheet-like and the intertrabecular spaces are smaller than in the uveal meshwork.
   c. ***The endothelial (juxtacanalicular) meshwork*** is the outer part of the trabeculum which links the corneoscleral meshwork with the endothelium of the inner wall of Schlemm canal (Fig. 9.2d). The juxtacanalicular tissue offers the major proportion of normal resistance to aqueous outflow.
2. **Schlemm canal** is a circumferential channel in the perilimbal sclera, bridged by septa. The inner wall of the canal is lined by irregular spindle-shaped endothelial cells which contain infoldings (giant vacuoles). The outer wall of the canal is lined by smooth flat cells and contains the openings of the collector channels (Fig. 9.2e) which leave Schlemm canal at oblique angles and connect directly or indirectly with episcleral veins.

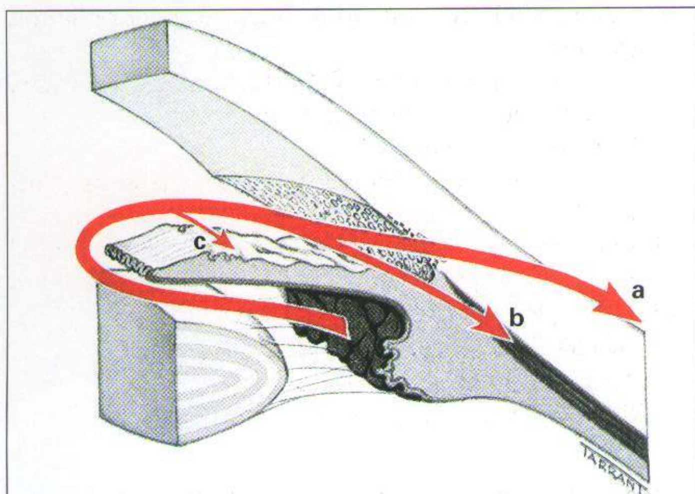


Fig. 9.3
Normal outflow of aqueous humour. (**a**) Conventional trabecular route; (**b**) uveoscleral route; (**c**) through the iris

Physiology

Aqueous flows from the posterior chamber via the pupil into the anterior chamber, from where it exits the eye by two different routes:

1. **Trabecular (conventional) route** accounts for approximately 90% of aqueous outflow (Fig. 9.3a). The aqueous flows through the trabeculum into Schlemm canal and is then drained by the episcleral veins. This is a bulk-flow pressure-sensitive route so that increasing the pressure head will increase outflow. Trabecular outflow can be increased by drugs (miotics, sympathomimetics), laser trabeculoplasty and trabeculotomy.
2. **Uveoscleral (unconventional) route** accounts for the remaining 10% of aqueous outflow (Fig. 9.3b). The aqueous passes across the face of the ciliary body into the suprachoroidal space and is drained by the venous circulation in the ciliary body, choroid and sclera. Uveoscleral outflow is decreased by miotics and increased by atropine, sympathomimetics and prostaglandins. Some aqueous also drains via the iris (Fig. 9.3c)

Intraocular pressure

Determining factors

1. **Rate of aqueous secretion**.
2. **Rate of aqueous outflow**, which is in turn related to the resistance encountered in the outflow channels and the level of episcleral venous pressure. The rate of aqueous outflow is proportional to the difference between the intraocular and episcleral venous pressure. The relationship between these factors can be expressed as follows:

   $F = C\,(Po - Pe)$ where:

   F = rate of aqueous outflow (normal 2 µl/min)
   C = facility of aqueous outflow (normal 0.2 µl/min per mmHg)
   Po = IOP in mmHg
   Pe = episcleral venous pressure (normal 10 mmHg)

   For example:

   - If episcleral venous pressure is 20 mmHg the IOP will be $(2/0.2) + 20 = 30$ mmHg.
   - If the facility of outflow is 0.05 the IOP will be $(2/0.05) + 10 = 50$ mmHg.

Distribution

The distribution of IOP within the general population has a range of 11–21 mmHg. Although there is no absolute cut-off point, 21 mmHg is considered the upper limit of normal and levels above this are viewed with suspicion. However, in some patients glaucomatous damage occurs with IOPs less than 21 mmHg (normal-tension glaucoma), while others remain unscathed with IOPs up to 30 mmHg (ocular hypertension). Although the actual level of IOP is important in the development of glaucomatous damage, other factors also play a part. The level of IOP is inherited so that first-degree relatives of patients with primary open-angle glaucoma have higher IOPs.

Fluctuation

Normal IOP varies with the time of day, heartbeat, blood pressure level and respiration. The pattern of diurnal curves of IOP varies, with a tendency to be higher in the morning and lower in the afternoon and evening. Normal eyes manifest a mean diurnal pressure variation of 5 mmHg; ocular hypertensive or glaucomatous eyes, however, exhibit a wider fluctuation. In normal-tension glaucoma the fluctuations are the same as in normals. A single normal reading, particularly if taken during late afternoon, may therefore be misleading and it may be necessary to take several readings at different times of day (phasing). In clinical practice phasing during the morning hours may be sufficient because 80% of patients peak between 8 and 12 a.m.

Classification

Glaucoma is an optic neuropathy with characteristic appearances of the optic disc and specific pattern of visual field defects that is associated frequently but not invariably with raised IOP. Because the pathophysiology, clinical presentation and treatment of the different types of glaucoma are so varied, there is no single definition that adequately encompasses all forms. Understanding this concept helps to explain, for example, why one patient with 'glaucoma' may have no symptoms while another experiences sudden pain and redness. Glaucoma may be (a) *congenital* (developmental) or (b) *acquired*. Further subclassification into open-angle and angle-closure types is based on the mechanism by which aqueous outflow is impaired. The glaucoma may also be (a) *primary* or (b) *secondary* depending on the presence or absence of associated factors contributing to the pressure rise. In primary glaucomas the elevation of IOP is not

associated with any other ocular disorder whereas in secondary glaucomas a recognizable ocular or non-ocular disorder alters aqueous outflow which, in turn, results in elevation of IOP. Secondary glaucomas may be acquired or developmental and of the open-angle or angle-closure type.

Secondary open-angle glaucomas

They can be subdivided on the basis of the site of aqueous outflow obstruction.

1. **Pre-trabecular** glaucoma in which aqueous outflow is obstructed by a membrane covering the trabeculum (Fig. 9.4a), which may consist of:
   - Fibrovascular tissue (e.g. neovascular glaucoma).
   - Endothelial cells (e.g. iridocorneal endothelial syndrome).
   - Epithelial cells (e.g. epithelial ingrowth).
2. **Trabecular** glaucoma in which the obstruction occurs as a result of 'clogging up' of the meshwork by:
   - Pigment particles (e.g. pigmentary glaucoma, Fig. 9.4b).
   - Red blood cells (e.g. red cell glaucoma).
   - Degenerated red cells (e.g. ghost cell glaucoma).
   - Macrophages and lens proteins (e.g. phacolytic glaucoma).
   - Proteins (e.g. hypertensive uveitis).
   - Pseudoexfoliative material (e.g. pseudoexfoliation glaucoma).

   Trabecular glaucomas may also be caused by alteration of the trabecular fibres themselves by:
   - Oedema (e.g. herpes zoster iritis).
   - Scarring (e.g. post-traumatic angle recession glaucoma).
3. **Post-trabecular** glaucoma in which the trabeculum itself is normal but aqueous outflow is impaired as a result of elevated episcleral venous pressure due to:
   - Carotid–cavernous fistulae.
   - Sturge–Weber syndrome.
   - Obstruction of the superior vena cava.

Secondary angle-closure glaucomas

These are caused by impairment of aqueous outflow secondary to apposition between the peripheral iris and the trabeculum by either posterior or anterior forces as follows:

1. **Posterior forces** push the peripheral iris against the trabeculum (e.g. iris bombé due to seclusio pupillae, (Fig. 9.4c)).
2. **Anterior forces** pull the iris over the trabeculum by contraction of inflammatory (Fig. 9.4d) or fibrovascular membranes (e.g. late neovascular glaucoma).

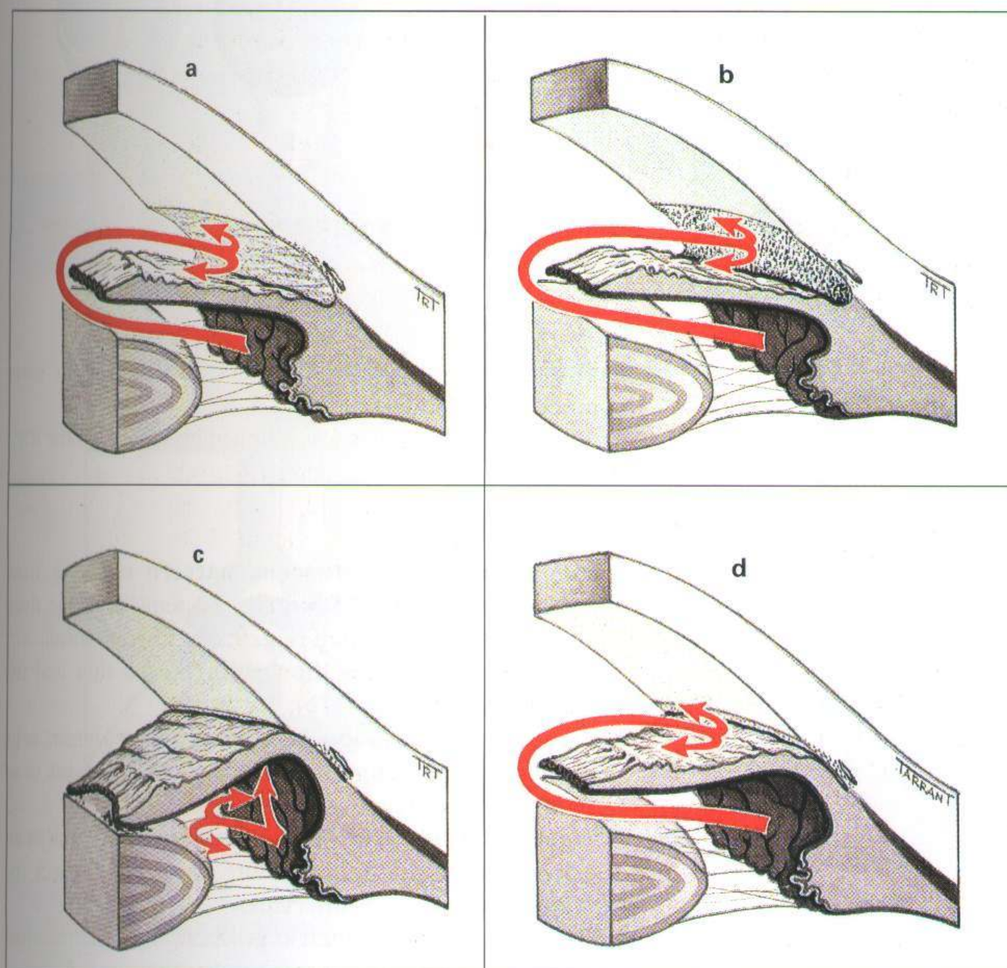


Fig. 9.4 Mechanism of aqueous obstruction in secondary glaucomas (*see* text)

Tonometry

Goldmann tonometry

General principles

Tonometry is the objective measurement of IOP, based, most commonly, on the force required to flatten the cornea, or the degree of corneal indentation produced by a fixed force. Applanation tonometry is based on the Imbert–Fick principle, which states that for an ideal, dry, thin-walled sphere, the pressure inside the sphere (P) equals the force necessary to flatten its surface (F) divided by the area of flattening (A) (i.e. $P = F/A$). The IOP is proportional to the pressure applied to the globe (in practice the cornea) and the thickness of the walls of the globe (i.e. the thickness of the cornea, which is variable). The human eye is, however, not an ideal sphere—the cornea is rigid and resists flattening. Capillary attraction of the tear meniscus however, tends to pull the tonometer towards the cornea. Corneal rigidity and capillary attraction cancel each other when the flattened area has a diameter of 3.06 mm, as in Goldmann tonometry (Fig. 9.5). The Goldmann tonometer is a very accurate variable-force tonometer consisting of a double prism (Fig. 9.6).

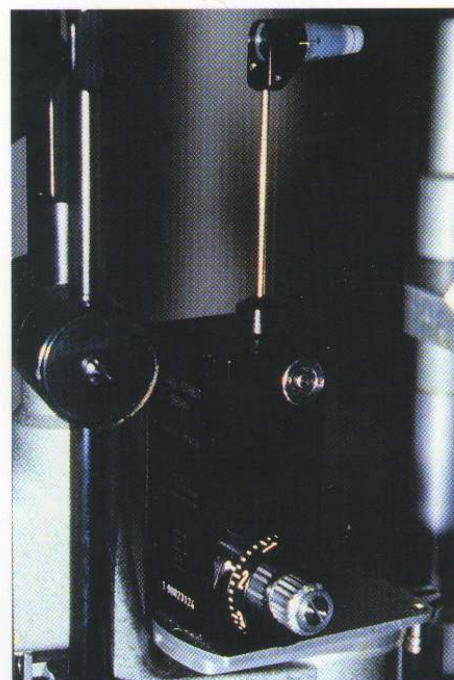


Fig. 9.6
Goldmann applanation tonometer

Procedure

1. Topical anaesthetic and fluorescein are instilled into the conjunctival sac.
2. At the slit-lamp, a Goldmann prism (mounted on a tonometer) is applied axially to the cornea surface.
3. A pattern of two semicircles will be seen, one above and one below the horizontal midline.

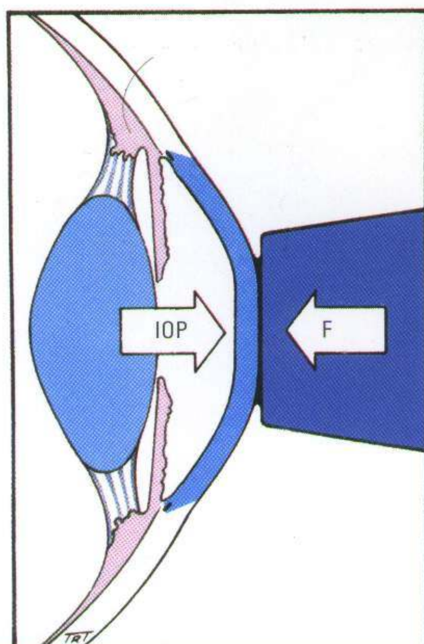


Fig. 9.5
Principles of Goldmann applanation tonometry

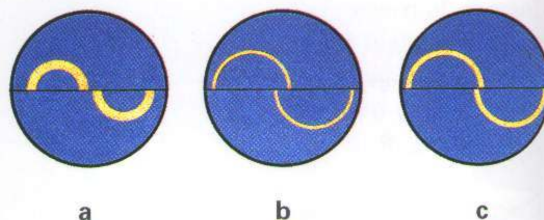


Fig. 9.7
Fluorescein-stained semicircles seen during tonometry (see text)

4. The dial on the tonometer is rotated to align the inner margins of the semicircles (Fig. 9.7c).
5. The reading on the dial, multiplied by 10, equals the IOP.

Potential errors

1. **Inappropriate fluorescein pattern** resulting from excessive fluorescein will make the semicircles too thick and the radius too small (Fig. 9.7a), whereas insufficient fluorescein will make the semicircles too thin and the radius too large (Fig. 9.7b).
2. **Pressure on the globe**, from the examiner's fingers or by the patient squeezing the eyelids (Fig. 9.8) will result in an artificially high reading.
3. **Incorrect calibration** of the tonometer can result in an incorrect reading. It is therefore important to check the calibration at regular intervals.
4. **Corneal pathology** such as gross oedema, distortion and abnormal thickness will result in inaccurate readings.

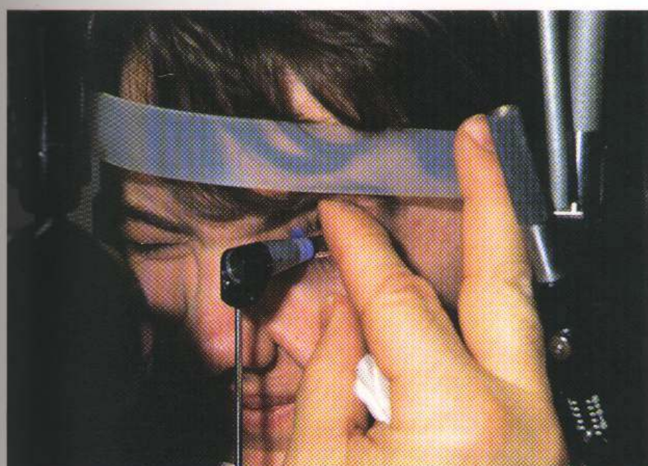


Fig. 9.8
Squeezing of the eyelids during tonometry will result in an inaccurate reading

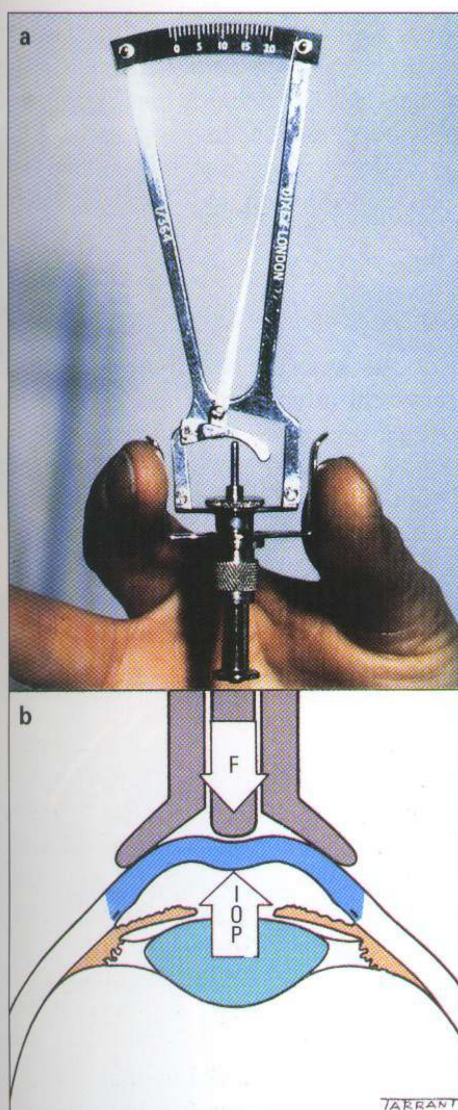


Fig. 9.9
(a) Schiotz tonometer; (b) principles of indentation tonometry

Other tonometers

1. **The Schiotz** relies on the principle of indentation tonometry in which a plunger with a pre-set weight indents the cornea (Fig. 9.9). The amount of indentation is measured on a scale and the reading is converted into millimetres of mercury on a special table. The tonometer is cheap, easy to use and does not require a slit-lamp but is now seldom used.
2. **The Perkins** is a hand-held applanation tonometer which uses a Goldmann prism adapted to a small light source. It is small, does not require a slit-lamp and can therefore be used in bed-bound or anaesthetized patients (Fig. 9.10). It does, however, require considerable practice before reliable readings can be obtained.
3. **The air-puff** (Fig. 9.11) is a non-contact tonometer based on the principle of applanation but, instead of using a prism, the central part of the cornea is flattened by a jet of air. The time required to sufficiently flatten the cornea relates directly to the level of IOP. The instrument is easy to use and does not require topical anaesthesia. It is therefore

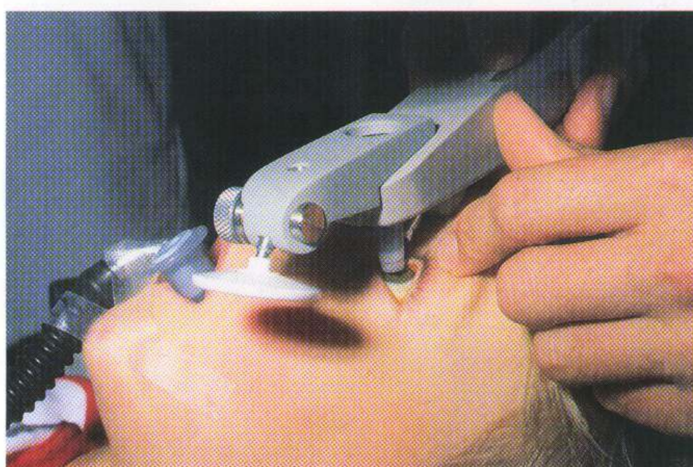


Fig. 9.10
Perkins hand-held applanation tonometer



Fig. 9.11
Air-puff tonometer


Fig. 9.12
Pulsair (Keeler) tonometer


Fig. 9.13
Tono-Pen

particularly useful for screening by non-ophthalmologists. Its main disadvantage is that it is accurate only within the low-to-middle range. The jet of air can startle the patient both with its apparent force and noise.

4. **The Pulsair 2000 Keeler** (Fig. 9.12) is a hand-held non-contact tonometer, incorporating an automatic alignment activation device which reduces user error. The instrument can be used with the patient in the upright and supine positions and does not make a noise. It provides clinically useful measurements comparable with Goldmann tonometry although with use a tendency to a long-term drift in accuracy mandates regular re-calibration.
5. **The Tono-Pen** is a hand-held, self-contained, battery powered, portable, contact tonometer (Fig. 9.13). The probe tip contains a transducer that measures the applied force. A microprocessor analyses the force/time curve generated by the transducer during corneal indentation to calculate IOP. The instrument correlates well with Goldmann tonometry although it slightly overestimates a low IOP and underestimates a high IOP. Its main advantage involves the ability to measure IOP in eyes with distorted or oedematous corneas, as well as through a bandage contact lens.

Gonioscopy

Introduction

Purposes

The angle between the posterior corneal surface and the anterior surface of the iris constitutes the angle of the anterior chamber, the configuration of which is relevant to the pathogenesis of glaucoma. Contact between peripheral iris and cornea signifies a closed angle, which precludes aqueous access to the trabecular meshwork, while wide separation between the two signifies an open angle, implying that the obstruction to aqueous outflow lies in or beyond the trabecular meshwork. Gonioscopy involves the examination and analysis of the angle.

1. **Diagnostic** gonioscopy facilitates the identification of abnormal angle structures and estimation of the width of the chamber angle, particularly important in the management of eyes with narrow angles.
2. **Surgical** gonioscopy involves visualization of the angle during procedures such as laser trabeculoplasty and goniotomy.

Optical principles

The angle of the anterior chamber cannot be visualized directly through the intact cornea because light emitted from angle structures undergoes total internal reflection at the anterior surface of the precorneal tear film. A goniolens eliminates total internal reflection by replacing the tear film–air interface with a new tear film–goniolens interface (Fig. 9.14).

1. **Indirect** goniolenses (goniomirrors) provide a mirror image of the opposite angle and can be used only in conjunction with a slit-lamp.

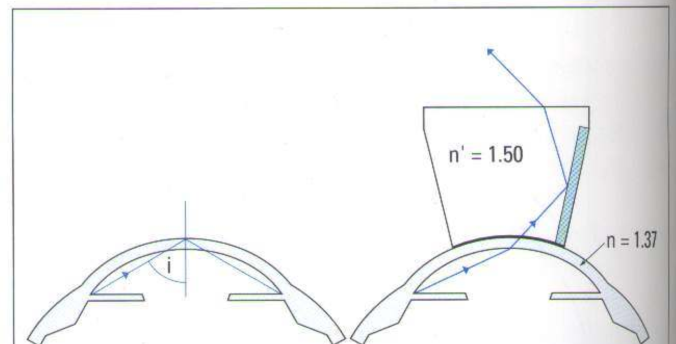


Fig. 9.14
Optical principles of gonioscopy: n = refractive index; i = angle of incidence

2. **Direct** goniolenses (gonioprisms) provide a direct view of the angle. They do not require a slit-lamp and are used with the patient in the supine position.

Goniolenses

Goldmann three-mirror

This is an indirect goniolens with a contact surface diameter of approximately 12 mm (Fig. 9.15 left). Relatively easy to master, it affords an excellent view of the angle. It also stabilizes the globe and is therefore suitable for argon laser trabeculoplasty. Because the curvature of the contact surface of the lens is steeper than that of the cornea a viscous coupling substance with the same refractive index as the cornea is required to bridge the gap between the cornea and the goniolens. Following the use of the coupling substance the patient's vision is blurred and fundus examination impaired. Perimetry, ophthalmoscopy or photography of the discs should therefore be performed before gonioscopy.

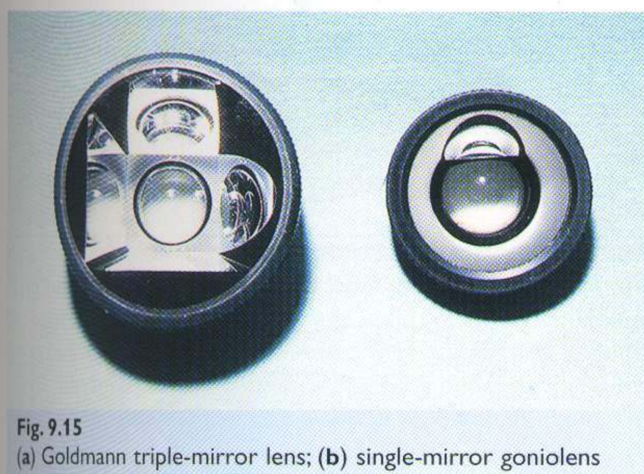


Fig. 9.15
(**a**) Goldmann triple-mirror lens; (**b**) single-mirror goniolens

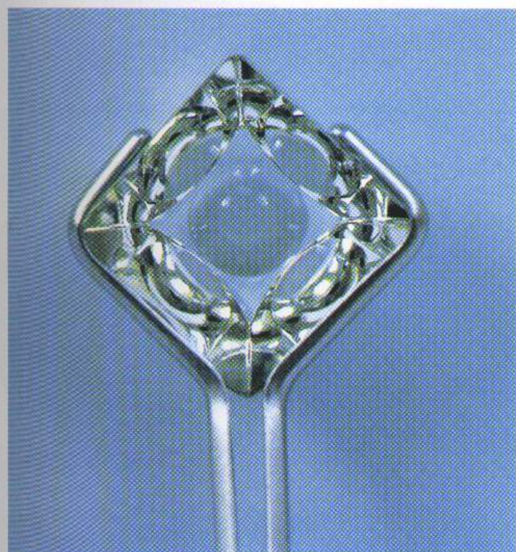


Fig. 9.16
Zeiss four-mirror goniolens

Modifications of the Goldmann lens with one (Fig. 9.15 right) and two mirrors and antireflective coating have been designed for laser trabeculoplasty, enabling simultaneous visualization of a wider circumference of the angle.

Zeiss

This and the similar Posner and Sussman, are indirect four-mirror goniolenses mounted on a handle (Fig. 9.16). The contact surface of the lens has a diameter of 9 mm and a curvature flatter than that of the cornea, negating the need for a coupling substance. Tears provide adequate contact material and lubrication for the lens. This permits quick and comfortable examination of the angle and, importantly, does not interfere with subsequent examinations of the fundus. The four mirrors enable the entire circumference of the angle to be visualized with minimal rotation. This lens is useful for indentation gonioscopy (*see* below), but because it does not stabilize the globe it cannot be used for laser trabeculoplasty.

Koeppe

This is a dome-shaped direct diagnostic goniolens which comes in several sizes (Fig. 9.17). It is easy to use and provides a panoramic view of the angle. It is therefore particularly



Fig. 9.17
Koeppe goniolenses



Fig. 9.18
Swan–Jacob surgical goniolens

useful for simultaneous comparison of one portion of the angle with another. Moreover, with the patient in the supine position the anterior chamber may become slightly deeper and the angle easier to visualize. When used in conjunction with a hand-held microscope, it offers great flexibility, allowing detailed inspection of the various subtleties of angle structures both by direct and retroillumination. It cannot be used in conjunction with a slit-lamp and therefore does not provide the same clarity, illumination and variable powers comparable with slit-lamp goniolenses.

Swan–Jacob

This is a direct surgical goniolens which is held on the cornea by a handle (Fig. 9.18).

Gonioscopic technique

Goldmann gonioscopy

The patient should be advised that the lens will touch the eye but not cause more than slight discomfort. The patient should also be requested to keep both eyes open at all times and not to move the head backwards when the lens is being inserted.

1. Topical anaesthetic is instilled into the lower fornix.
2. A coupling fluid (e.g. a carbomer gel) is inserted into the cup of the lens but it should be no more than half full.
3. The patient looks up and the inferior rim of the lens is inserted into the lower fornix and then pressed quickly against the cornea so that the coupling substance does not escape. The patient is then asked to gaze straight ahead with the other eye.
4. The angle is visualized with the small dome-shaped gonioscopic mirror (if a three-mirror lens is being used).
5. Initially the mirror is placed at the 12 o'clock position to visualize the inferior angle and then rotated clockwise. The slit beam should be 2 mm wide and when viewing different positions it is usually best to rotate the beam so that its axis is at right angles to the mirror.

> ***NB:*** The image is laterally reversed with the mirror in the horizontal meridian and vertically inverted when in the vertical meridian.

Zeiss gonioscopy

The preliminary steps are the same as for Goldmann gonioscopy but a coupling fluid is not required.

1. The patient looks straight ahead. Under slit-lamp visualization the lens is placed directly on the centre of the cornea. Only gentle contact with the cornea is needed because excessive pressure will inadvertently distort angle structures.
2. Each quadrant of the angle is visualized with the opposite mirror. The central fundus may be viewed through the centre of the lens.
3. Indentation gonioscopy may be performed by pressing posteriorly against the cornea. This will force aqueous into the angle of the anterior chamber, forcing the peripheral iris posteriorly.
   - If the angle is closed by mere apposition between the iris and cornea (appositional closure), the angle will be forced open, allowing visualization of the angle recess (Fig. 9.19b).
   - If the angle is completely closed by adhesions between the peripheral iris and cornea (synechial closure) it will remain closed (Fig. 9.19c).

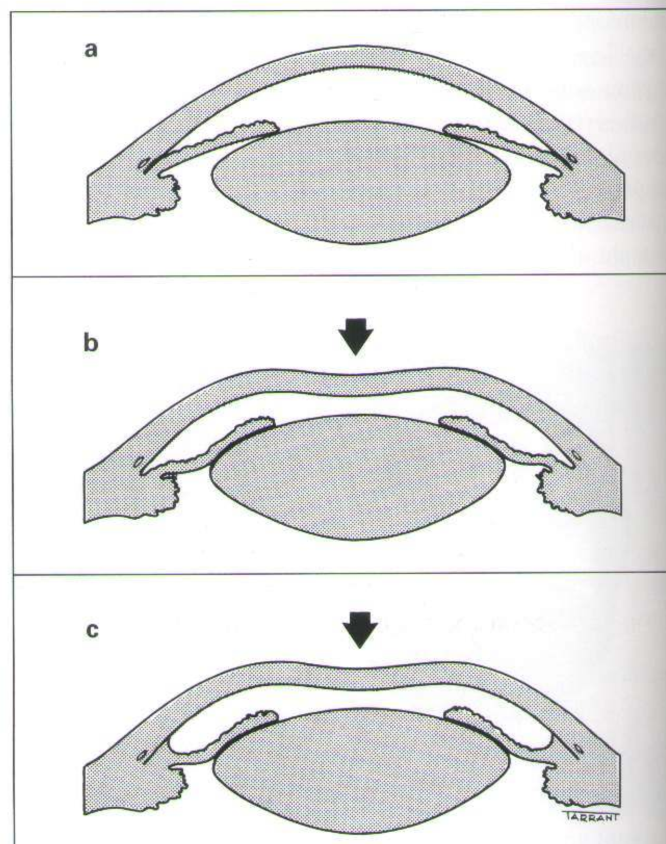


Fig. 9.19
Principles of indentation gonioscopy (*see text*)

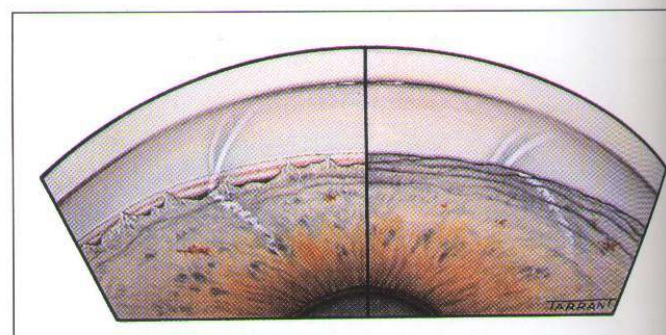


Fig. 9.20
Indentation gonioscopy. (**Right**) appearance of the angle before indentation showing complete closure and inability to visualize the apex of the corneal wedge; (**left**) during indentation part of the angle is forced open but some permanent peripheral synechiae remain

- If synechial closure is partial, part of the angle will open and a part will remain closed (Fig. 9.20 left).

> *NB:* With practice, gentle indentation gonioscopy allows better visualization even of the normal angle. Gonioslenses are a potential source of infection and should be disinfected in the same way as tonometer heads.

Identification of angle structures

Figure 9.21 shows the anatomy of angle structures.

1. **Schwalbe line** is the most anterior structure, appearing as an opaque line. Anatomically it demarcates the peripheral termination of Descemet membrane and the anterior limit of the trabeculum.
2. **The corneal wedge** is useful in locating an inconspicuous Schwalbe line as follows:
   a. Using a narrow slit beam, two linear reflections can be seen, one from the external surface of the cornea and its junction with the sclera, the other from the internal surface of the cornea.
   b. The two reflections meet at the apex of the corneal wedge, which coincides with Schwalbe line.

> *NB:* When performing laser trabeculoplasty a pigmented Schwalbe line should not be confused with the posterior pigmented trabeculum.

3. **The trabeculum** extends from Schwalbe line to the scleral spur and has an average width of 600 μm. Gonioscopically, it has a ground-glass appearance and appears to have depth. The anterior non-functional part lies adjacent to Schwalbe line and has a whitish colour. The posterior functional pigmented part lies adjacent to the scleral spur and has a greyish-blue translucent appearance. In laser trabeculoplasty burns are applied at the junction of the non-pigmented and pigmented trabeculum. Trabecular pigmentation (Fig. 9.22) is rare prior to puberty. In ageing eyes it involves the posterior trabeculum to a variable extent, most marked inferiorly and least in the horizontal meridian. Trabecular pigmentation is also most marked in brown eyes. Pathological hyperpigmentation is caused by excessive shedding of pigment from the posterior layer of the iris in the following conditions:
   - Pigment dispersion syndrome.
   - Pseudoexfoliation syndrome.
   - Blunt ocular trauma.
   - Anterior uveitis.
   - Following acute angle-closure glaucoma.
   - Diabetes (especially after cataract surgery).
   - Naevus of Ota.

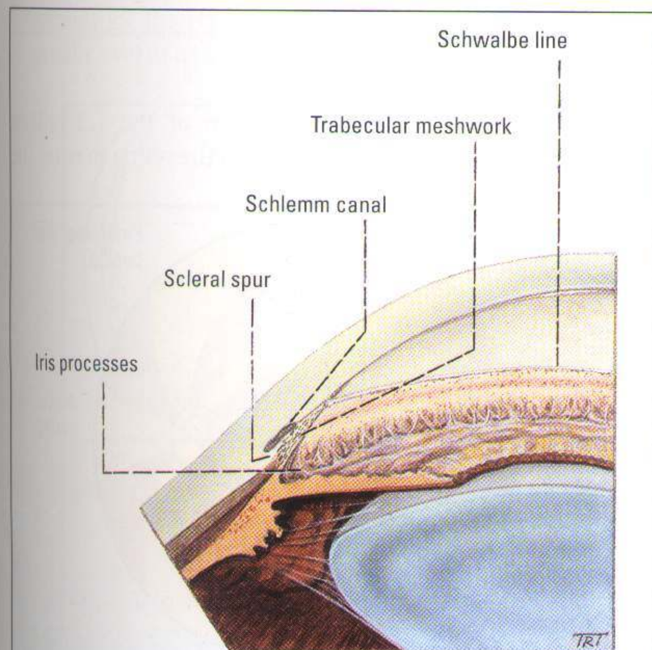


Fig. 9.21
Anatomy of the angle structures



Fig. 9.22
Wide open angle with trabecular pigmentation

4. **Schlemm canal** may be identified in the non-pigmented angle as a slightly darker line deep to the posterior trabeculum. Blood can sometimes be seen in this canal if the goniolens compresses the episcleral veins such that the episcleral venous pressure exceeds the IOP. Pathological causes of raised episcleral venous pressure which may be associated with blood in Schlemm canal include:
   - Carotid–cavernous fistula and dural shunt.
   - Sturge–Weber syndrome.
   - Obstruction of the superior vena cava.
5. **The scleral spur** is the anterior-most projection of the sclera and the site of attachment of the longitudinal muscle of the ciliary body. Gonioscopically, the scleral spur is situated immediately posterior to the trabeculum and appears as a narrow, dense, often shiny, whitish band. It is the most important landmark because it has a relatively consistent appearance in different eyes.

> *NB:* In laser trabeculoplasty it is important to identify the scleral spur because the application of burns posterior to it will result in greater inflammation, with consequent increased risk of early post-laser rise in IOP and the formation of peripheral anterior synechiae.

6. **The ciliary body** stands out just behind the scleral spur as a pink to dull-brown to slate-grey band. Its width depends on the position of iris insertion and it tends to be narrower in hypermetropic eyes and wider in myopic eyes. The angle recess represents the posterior dipping of the iris as it inserts into the ciliary body.
7. **Iris processes** are small extensions of the anterior surface of the iris which insert at the level of the scleral spur and cover the ciliary body in varying degrees. They are present in about one-third of normal eyes and are most prominent during childhood and in brown eyes. With increasing age they tend to wither and lose their continuity. Iris processes should not be confused with peripheral anterior synechiae, which are broader and represent adhesions between the iris and angle structures. However, fine stellate peripheral anterior synechiae induced by inappropriate laser trabeculoplasty may easily be mistaken for iris processes.
8. **Blood vessels** running in a radial pattern at the base of the angle recess are often seen in normal eyes. Pathological blood vessels, which run randomly in various directions, occur in:
   - Neovascular glaucoma.
   - Fuchs uveitis syndrome.
   - Chronic anterior uveitis.

Grading of angle width

Grading of angle width is essential to the assessment of the glaucomatous or potentially glaucomatous eye. The main aims are to evaluate the functional status of the angle, the degree of closure and the risk of future closure. The following features should be noted and described in the superior and inferior halves of the angle, bearing in mind that most angles are narrowest superiorly.

- The shape and contour of the peripheral iris.
- The deepest structure seen.
- Amount of trabecular pigmentation.
- Presence of peripheral anterior synechiae.

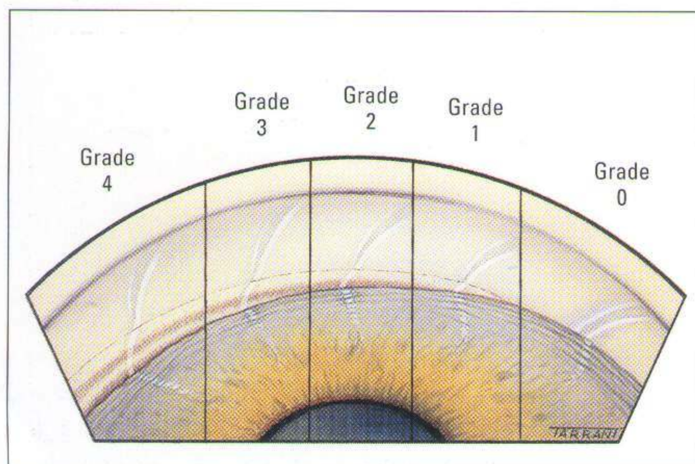


Fig. 9.23
Shaffer grading of angle width

The Shaffer system (Fig. 9.23) records the angle in degrees of arc subtended by two imaginary tangential lines drawn to the inner surface of the trabeculum and the anterior surface of the iris about one-third of the distance from its periphery. In practice, the angle is graded according to the visibility of various angle structures. The system assigns a numerical grade (4–0) to each angle with associated anatomical description, angle width in degrees and implied clinical interpretation.

1. **Grade 4** (35–45°) is the widest angle characteristic of myopia and aphakia in which the ciliary body can be visualized with ease; it is incapable of closure.
2. **Grade 3** (25–35°) is an open angle in which at least the scleral spur can be identified; it is also incapable of closure.
3. **Grade 2** (20°) is a moderately narrow angle in which only the trabeculum can be identified; angle closure is possible but unlikely.
4. **Grade 1** (10°) is a very narrow angle in which only Schwalbe line, and perhaps also the top of the trabeculum, can be identified; angle closure is not inevitable but the risk is high.
5. **Slit angle** is one in which there is no obvious iridocorneal contact but no angle structures can be identified; this angle has the greatest danger of imminent closure.
6. **Grade 0** (0°) is a closed angle due to iridocorneal contact and is recognized by the inability to identify the apex of the corneal wedge. Indentation gonioscopy with a Zeiss goniolens is necessary to differentiate 'appositional' from 'synechial' angle closure as previously described.

The optic nerve head

Applied anatomy

Retinal nerve fibres

An understanding of the distribution of the 1.2 million ganglion cell axons as they pass across the retina to enter the

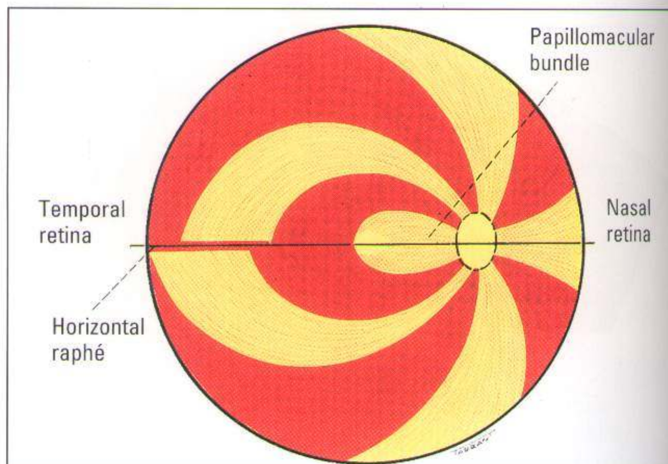


Fig. 9.24
Anatomy of retinal nerve fibres

scleral canal to form the optic nerve head (optic disc) is the key to the interpretation of visual field loss in relation to optic nerve cupping in glaucoma.

1. **Within the retina** the arrangement is as follows (Fig. 9.24):
   - Fibres arising from the macula follow a straight course to the optic nerve head, forming a spindle-shaped area (papillomacular bundle).
   - Fibres arising from the nasal retina also follow a relatively straight course to the optic nerve.
   - Fibres arising temporal to the macula follow an arcuate path around the papillomacular bundle to reach the optic nerve head. They do not cross the horizontal raphé that extends from the foveola to the temporal retinal periphery, demarcating the superior and inferior halves of the retina.

> ***NB:*** The arcuate fibres reaching the superotemporal and inferotemporal aspects of the optic nerve head are most vulnerable to glaucomatous damage; the fibres in the papillomacular bundle are the most resistant.

2. **Within the optic nerve head** the retinal fibres are arranged as follows (Fig. 9.25):
   - Fibres from the peripheral fundus lie deep within the retinal nerve fibre layer (i.e. nearer the pigment epithelium) but occupy the most peripheral (superficial) portion of the optic nerve.
   - Fibres arising near to the optic nerve lie superficially within the nerve fibre layer (i.e. nearer the vitreous) but they occupy the central (deep) portion of the optic nerve.

Optic nerve head

1. **The posterior scleral foramen** (scleral canal) is the conduit for the retinal nerve fibres leaving the eye. It is usually oval in its vertical axis and has an average vertical diameter of 1.75 mm, which is, however, related to the size of the optic disc and the globe itself. Eyes with small canals therefore have small optic discs (e.g. hypermetropia) and those with large canals have large discs (e.g. myopia). Variations in the mode of scleral entry of the optic nerve give rise to anomalous congenital optic disc appearances, particularly tilted discs.
2. **The lamina cribrosa** consists of a series of plates of collagenous connective tissue which stretch across the posterior scleral foramen. It is perforated by 200–400 openings (pores) containing bundles of retinal nerve fibres. The largest pores are arranged in a vertical hourglass distribution at the superior and inferior poles, have thin connective tissue supports and contain large nerve fibres which are most vulnerable to glaucomatous damage. The superficial openings of the pores appear as grey dots deep within the optic cup. The appearance of the pores correlates with the severity of glaucomatous damage. If the damage is slight the pores are small and round, in moderately damaged eyes they are oval and in severe damage they are slit-like (*see* Fig. 9.37).

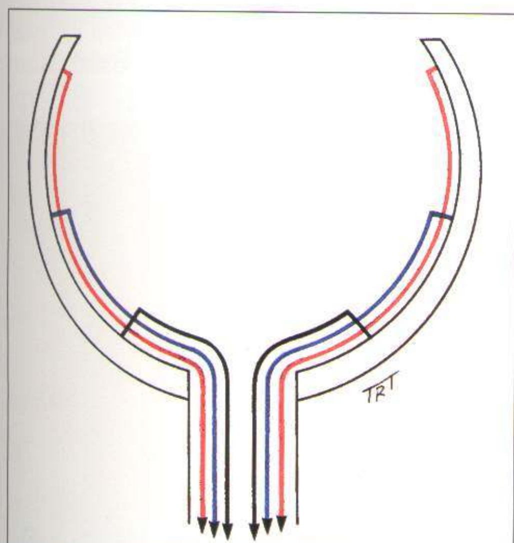


Fig. 9.25
Relative positions of retinal nerve fibres. (**Red**) peripheral; (blue) equatorial; (**black**) central

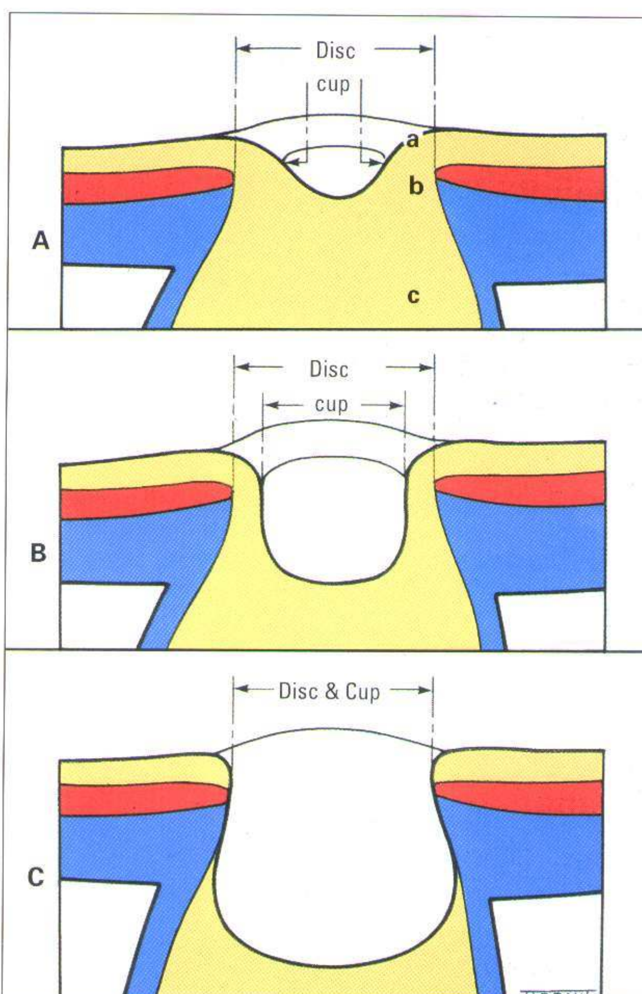


Fig. 9.26
Cross-section of the optic nerve head. (**A**) Small physiological cup: **a** = prelaminar layer, **b** = laminar layer, **c** = postlaminar layer; (**B**) large physiological cup; (**C**) total glaucomatous cupping

3. **The optic cup** is a pale depression in the centre of the optic nerve head which is not occupied by neural tissue. On direct ophthalmoscopy, it is best evaluated by observing the bending of the small blood vessels as they cross the disc, although on slit-lamp indirect ophthalmoscopy the actual borders of the cup may be appreciated three-dimensionally. The pallor of the cup results from exposure of the lamina cribrosa and lack of glial tissue in the centre of the disc. The size of the cup is related to the diameter of the disc. A small disc will have a small cup because the nerve fibres are crowded as they leave the eye, while a large disc will have a larger cup because the retinal nerve fibres are less crowded.
4. **Layers** (Fig. 9.26)
   a. The nerve fibre layer, the most superficial, is supported by astrocytes. It is readily visible ophthalmoscopically and is best visualized with red-free light.
   b. The prelaminar layer, consisting of retinal nerve fibres angling posteriorly from the plane of the retina, is visible only within the central cup (a in Fig. 9.26A).
   c. The laminar layer consists of the lamina cribrosa through which pass the retinal nerve fibres. The grey spots visible in the optic cup on ophthalmoscopy represent the anterior openings of the fenestrations in the lamina (b in Fig. 9.26A).
   d. The postlaminar layer consists of optic nerve posterior to the lamina cribrosa (c in Fig. 9.26A). The nerve fibres acquire myelin sheaths, due to which the diameter of the optic nerve doubles.

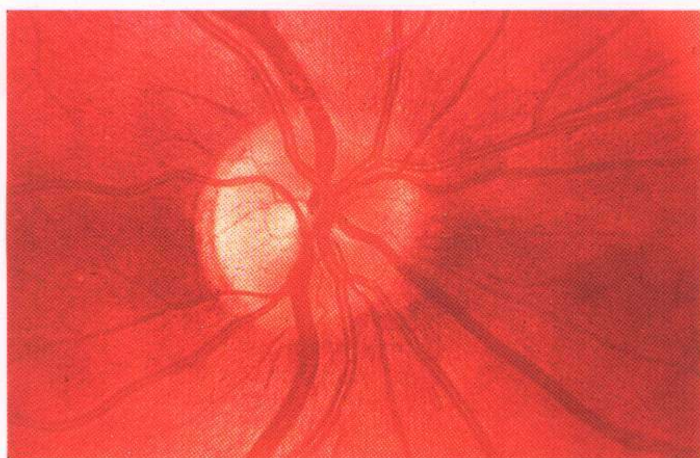


Fig. 9.27
Normal disc with a small (dimple) cup

The normal optic nerve head

1. **The optic cup** may have three main appearances:
   - A dimple-like small central cup (Fig. 9.27).
   - A punched-out deep central cup (Fig. 9.28).
   - A cup with a sloping temporal wall (Fig. 9.29).
2. **The cup:disc ratio** indicates the diameter of the cup expressed as a fraction of the diameter of the disc and should be measured in both vertical and horizontal meridia. This ratio is genetically determined and is also dependent on the area of the disc. The neuroretinal rim (*see* below) occupies a relatively similar area in different eyes; large discs therefore have large cups with high cup–disc ratios. Most normal eyes have a vertical cup–disc ratio of 0.3 or less; only 2% have a ratio greater than 0.7. A ratio greater than 0.7 should therefore be regarded with suspicion although it may not necessarily be pathological. In any individual, asymmetry of 0.2 or more between the eyes should also be regarded with suspicion until glaucoma has been excluded.
3. **The neuroretinal rim** is the tissue between the outer edge of the cup and the disc margin. The normal rim has an orange or pink colour and shows a characteristic configuration. The inferior rim is the broadest, followed by superior, nasal and temporal (ISNT). A large physiological cup is due to a mismatch between the size of the scleral canal and the number of traversing nerve fibres which in health remains constant (*see* Fig. 9.26B). Pathological cupping is caused by an irreversible decrease in the number of nerve fibres, glial cells and blood vessels (*see* Fig. 9.26C).
4. **The blood vessels** from within the optic nerve enter the disc centrally and then course nasally following the edge of the cup. The central retinal artery is usually nasal to the vein.

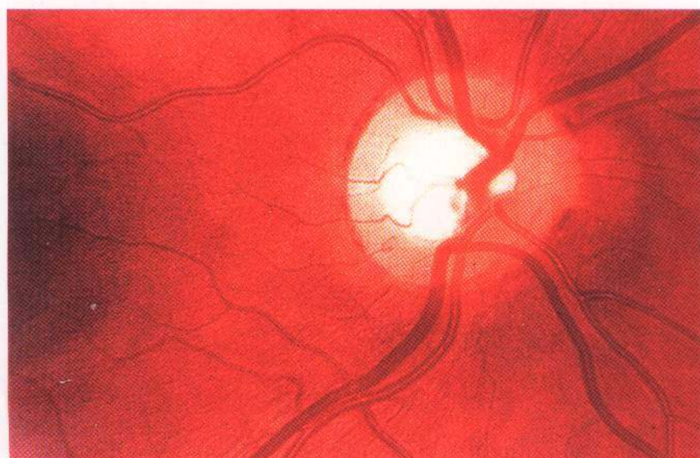


Fig. 9.28
Normal disc with a punched-out cup

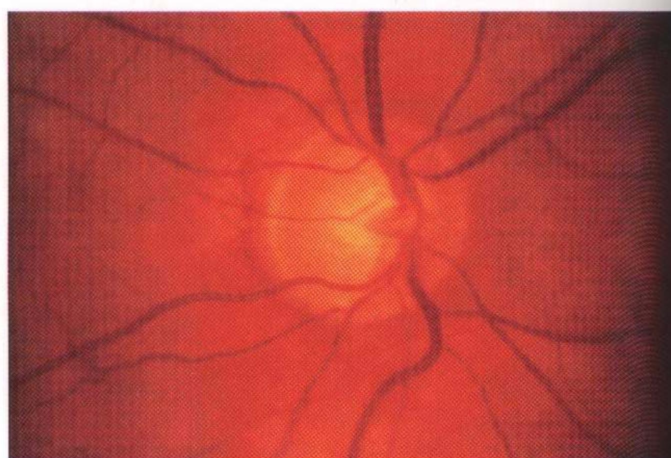


Fig. 9.29
Normal disc with a sloping temporal wall

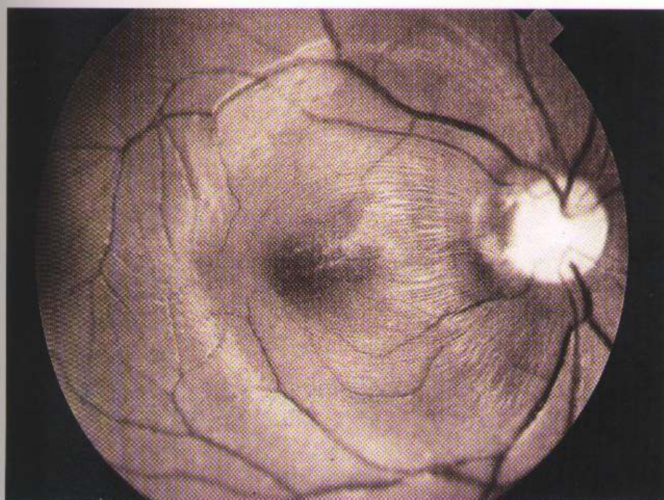


Fig. 9.30
Normal retinal nerve fibre layer, best seen with a green filter (Courtesy of J. Salmon)



Fig. 9.32
Diffuse nerve fibre atrophy in advanced glaucoma. No striations are visible and the retinal blood vessels appear dark and sharply defined (Courtesy of J. Salmon)

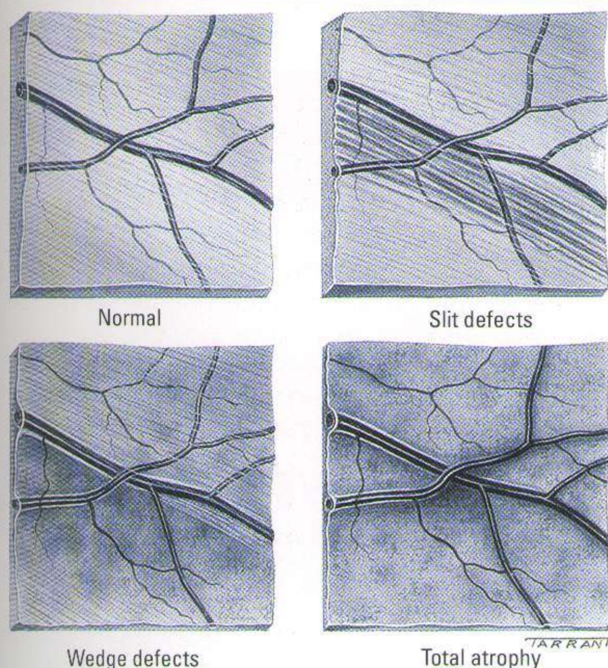


Fig. 9.31
Progression of glaucomatous retinal nerve fibre layer damage

Glaucomatous damage

Glaucomatous damage results in characteristic signs involving (a) *the retinal nerve fibre layer*, (b) *the optic nerve head* and (c) *the parapapillary area*.

Retinal nerve fibre damage

Figure 9.30 shows a normal retinal nerve fibre layer visualized with red-free light (a green filter). In glaucoma subtle retinal nerve fibre layer defects precede the development of detectable optic disc and visual field changes. Retinal nerve fibre dropout may be diffuse or localized. Early localized damage is characterized by slit or wedge-shaped defects in the retinal nerve fibre layer. As glaucomatous damage progresses the defects become larger; in end-stage glaucoma there is total atrophy of the nerve fibre layer characterized by complete baring of the larger retinal blood vessels, which run in this layer (Fig. 9.31). The atrophic area appears darker and mottled because of enhanced visualization of the retinal pigment epithelium (Fig. 9.32).

Optic disc damage

Optic disc damage is superimposed upon physiological cupping present prior to the onset of raised IOP. If an eye with a small cup develops glaucoma, the cup will increase in size, but during the early stages its dimensions may still be smaller than that of a large physiological cup. An estimation of cup size alone is therefore of limited value in the diagnosis of early glaucoma, unless it is found to be increasing. Glaucomatous cups are usually larger than physiological cups, although a large cup is not necessarily pathological. Assessment of the thickness, symmetry and colour of the neuroretinal rim is, however, more important. The spectrum of disc damage in glaucoma ranges from highly localized tissue loss with notching of the neuroretinal rim to diffuse concentric enlargement of the cup. Optic disc appearance is classified as follows:

1. **Type I** (focal ischaemic) disc is characterized by focal tissue loss at the superior and/or inferior poles (polar notching) and an otherwise relatively intact neuroretinal rim (Fig. 9.33). The notch is often associated with small areas of parapapillary atrophy or choroidal sclerosis (fundus tessellation). This type of disc tends to occur in older patients, particularly females, and is associated with localized field defects, with early threat to fixation. Particular attention should therefore be paid to neural tissue loss, in the vertical sectors of the cup.

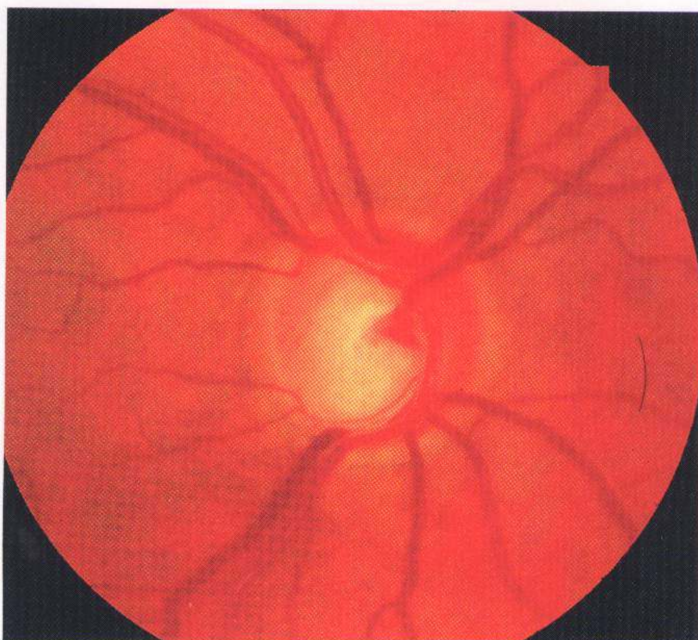


Fig. 9.33
Focal ischaemic glaucomatous damage

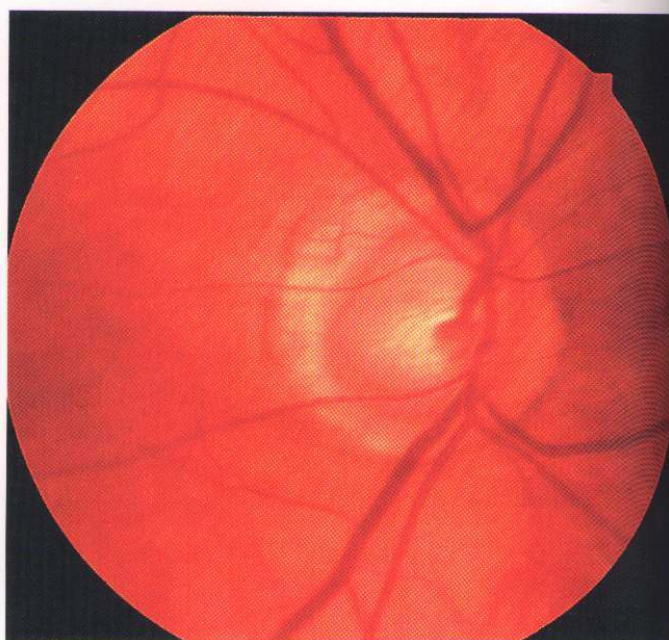


Fig. 9.35
Senile sclerotic glaucomatous disc

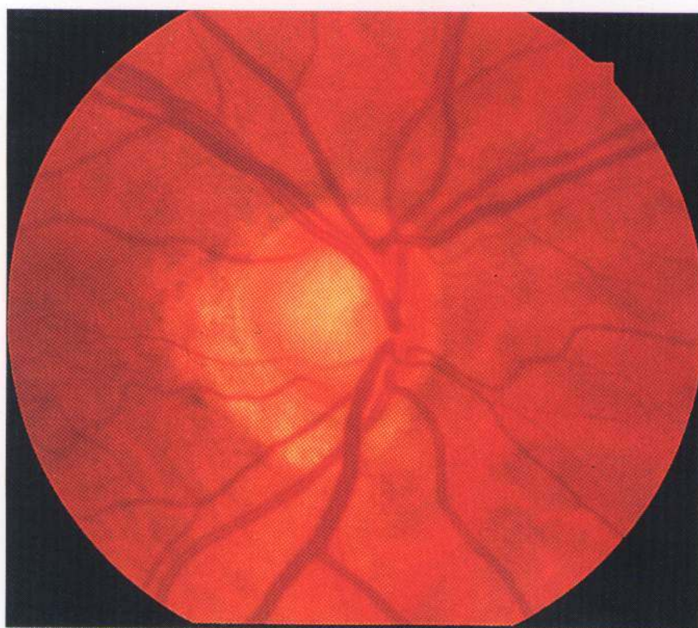


Fig. 9.34
Myopic glaucomatous disc

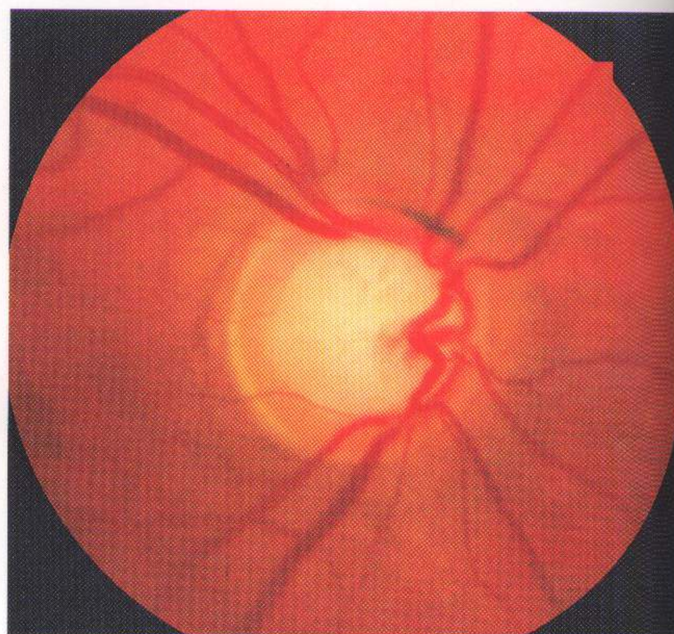


Fig. 9.36
Concentric glaucomatous enlargement

2. **Type 2** (myopic glaucomatous) disc is characterized by polar notching and a large temporal crescent in the absence of degenerative myopia (Fig. 9.34). It tends to occur in younger patients, particularly males, and is associated with localized visual field defects.
3. **Type 3** (senile sclerotic) disc is characterized by a shallow, saucerized cup and gently sloping neuroretinal rim, a 'moth-eaten appearance' and parapapillary atrophy or choroidal sclerosis surrounding the circumference of the nerve (Fig. 9.35). It tends to affect older patients and is associated with ischaemic heart disease and hypertension.
4. **Type 4** (concentric enlargement) disc is caused by diffuse loss of nerve fibres involving the entire cross-section of the optic nerve head, which results in a uniformly enlarged, round cup with no localized thinning of the neuroretinal rim (Fig. 9.36). This type of disc tends to occur in younger patients and is frequently associated with higher IOP and diffuse visual field loss. It may be very difficult to distinguish from a large physiological cup where the cup–disc diameter is still within normal limits. The best way to detect concentric enlargement of the cup is to compare it with a previous record.

Progression of glaucomatous damage

Figure 9.37 shows the progression of changes involving the optic disc and retinal nerve fibre layer.

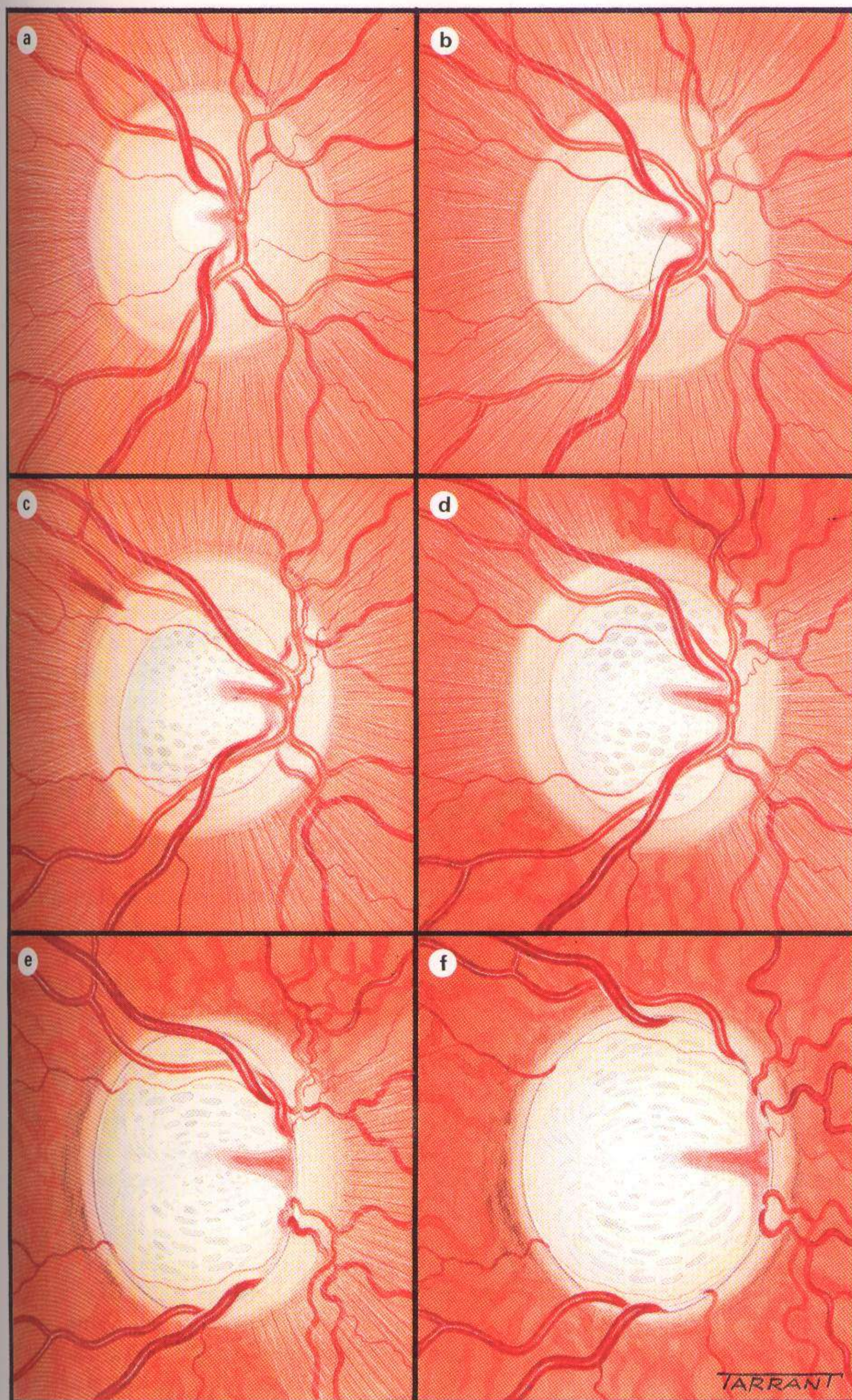


Fig. 9.37
Progression of glaucomatous optic nerve damage (*see text*)

- Figure 9.37a shows a normal disc with a small physiological cup and a cup–disc ratio of 0.2
- Figure 9.37b shows concentric enlargement and an increase in cup disc ratio to 0.5. The pores in the lamina cribrosa are small and round.
- Figure 9.37c shows inferotemporal expansion of the cup and a splinter-shaped haemorrhage on the disc margin, a frequent sign of imminent damage. There is corresponding loss of the inferior retinal nerve fibre layer and the pores in the inferior part of the cup are larger and oval.
- Figure 9.37d shows superior expansion of the cup so that it has become vertically oval. There is associated superior retinal nerve fibre loss and the pores in the superior lamina cribrosa are oval.

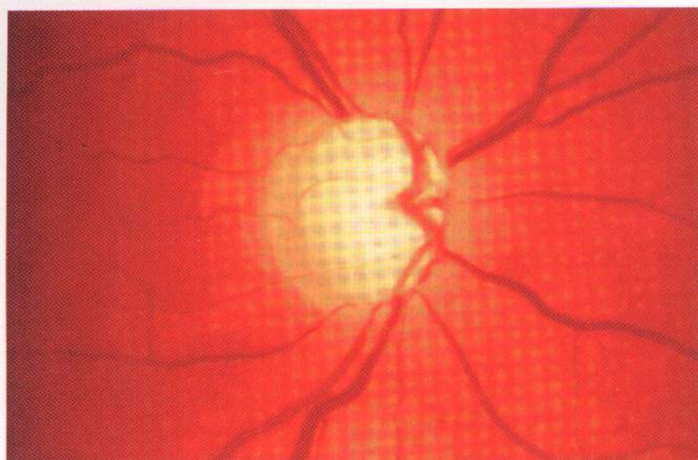


Fig. 9.38
End-stage glaucomatous cupping

- Figure 9.37e shows advanced cupping with total loss of superior, inferior and temporal disc tissue. There is associated retinal nerve fibre loss and the pores in the lamina cribrosa are slit-like. The progressive loss of nasal disc tissue has nasally displaced the central blood vessels emerging from the disc.
- Figures 9.37f and 9.38 show total cupping in which all neural disc tissue is destroyed and the optic nerve head appears white, deeply excavated with slit-like pores in the lamina cribrosa.

Parapapillary atrophy

Chorioretinal atrophy surrounding the optic nerve head is common in high myopia and may also occur in some healthy emmetropic eyes. There is, however, also a correlation between parapapillary atrophy and glaucoma. Atrophy surrounding the optic disc is conceptualized as consisting of two zones: an inner 'beta' zone, bordering the disc margin, which in turn is concentrically surrounded by an outer 'alpha' zone.

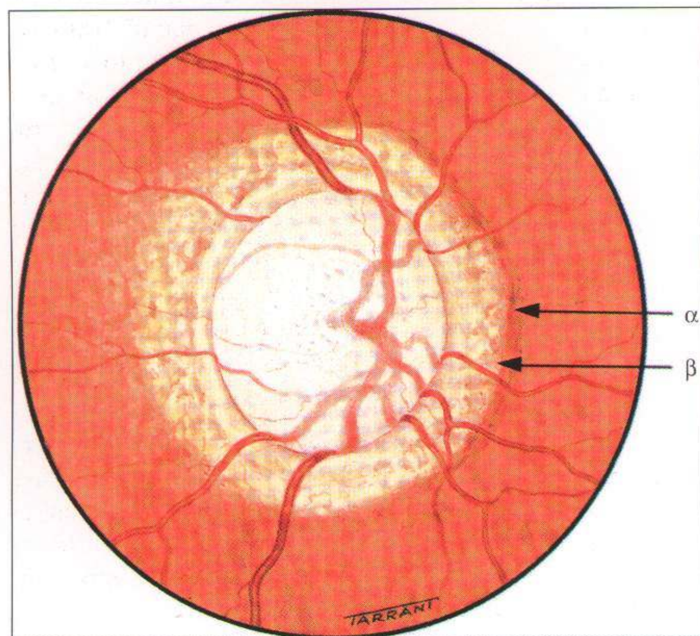


Fig. 9.39
Advanced glaucomatous cupping associated with parapapillary changes; a peripheral alpha zone and a central beta zone

1. **Signs** (Fig. 9.39)
   a. *The beta zone* exhibits chorioretinal atrophy with visibility of the sclera and large choroidal blood vessels.
   b. *The alpha zone* displays variable irregular hyper- and hypopigmentation of the retinal pigment epithelium.
2. **Significance**. The alpha zone is larger in patients with POAG but its frequency is similar in glaucomatous and normal subjects. However, the beta zone is not only larger but also occurs more frequently in patients with POAG than in normal individuals. In unilateral POAG, the changes are more advanced in the affected eye. In ocular hypertension, the presence and size of parapapillary changes correlates with the subsequent development of optic disc and visual field damage. Approximately half of all ocular hypertensive eyes that convert to POAG exhibit progression of parapapillary atrophic changes.

Imaging techniques

A decade ago, fundus photography was the only method to document optic disc changes in glaucoma. Since then, sophisticated electronic devices have been developed with a view to offering an objective, quantitative, specific and reproducible method to diagnose glaucoma and monitor its progression. Although they provide information on optic nerve head topography and/or parapapillary retinal nerve fibre thickness, each device has specific advantages and limitations and is at different stages of development.

1. **The Heidelberg retinal tomograph** is a confocal laser scanning microscope designed for three-dimensional imaging of the posterior segment of the eye. Due to its ability to produce highly accurate and reproducible images, this sophisticated technology can most effectively be applied to the evaluation of the fundus at or around the optic nerve head. It does not, however, provide a direct measurement of retinal nerve fibre layer thickness.
2. **Optical coherence tomography** (OCT) provides high-resolution cross-sectional images of the retina. Analogous to B scan ultrasonography, which utilizes sound waves, OCT uses light from a superluminescent diode. Optical coherence tomographs can discriminate the cross-sectional morphological features of the fovea (*see* Fig. 13.71) and optic disc, the layered structure of the retina, and normal anatomical variations in retinal and retinal nerve fibre layer thickness with a resolution of 10 μm. In glaucoma, retinal nerve fibre thickness is measured at standardized locations around the optic nerve head. Additional radial scans through the optic nerve head afford the evaluation of cupping and juxtapapillary retinal nerve fibre layer thickness. A large pupil and clear media are required for accurate measurements.

3. **Scanning laser polarimetry** (the Nerve Fibre Analyser) is based on the assumption that the retinal nerve fibre layer has birefringent properties. The change in polarization, called retardation, can be quantified by determining the phase shift between polarization of light returning from the eye with that of the illuminating laser beam. The degree of retardation is linearly related to retinal nerve fibre thickness.

NB: Currently, these techniques are still largely in the experimental stages. Conventional disc photography still remains the examination of choice in routine glaucoma practice.

Perimetry

Introduction

Definitions

1. **The visual field** may be described as an island of vision surrounded by a sea of darkness (Fig. 9.40). It is not a flat plane but a three-dimensional structure akin to a hill of vision. The outer aspect of the visual field extends approximately 50° superiorly, 60° nasally, 70° inferiorly and 90° temporally. Visual acuity is sharpest at the very top of the hill (i.e. the fovea) and then declines progressively towards the periphery, the nasal slope being steeper than the temporal. The blind spot is located temporally between 10° and 20°.

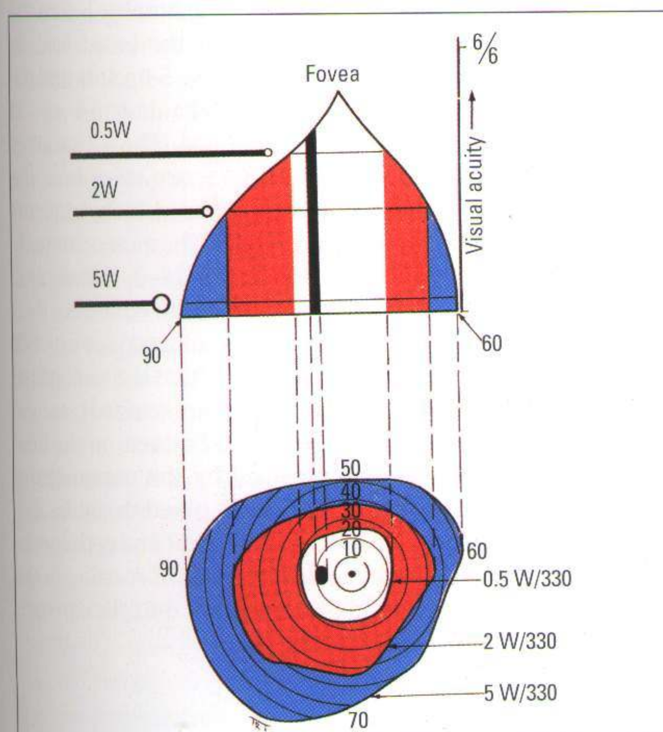


Fig. 9.40
Visual field and isopters. 0.5 W/330 = 0.5 mm white target at 0.33 metre; 2 W/330 = 2 mm white target at 0.33 metre; 5 W/330 = 5 mm white target at 0.33 metre

2. **An isopter**. As the size and luminance of a target are decreased, the area within which it can be perceived becomes smaller, so that a series of ever-diminishing circles called isopters is formed. Isopters therefore resemble the contour lines on a map which enclose an area within which a target of a given size is visible. An erosion of the 'coastline' of the island will therefore cause an indentation of all isopters in the affected area.
3. **A scotoma** is an area of visual loss, surrounded by vision.
   a. *An absolute* scotoma represents total loss of vision. Even the largest and brightest target cannot be perceived.
   b. *A relative* scotoma is an area of partial visual loss within which brighter or larger targets can be seen and smaller or dimmer ones cannot. A scotoma may have sloping edges so that an absolute scotoma is surrounded by a relative scotoma.
4. **Luminance** is the intensity or 'brightness' of a light stimulus, measured in apostilb (asb). A decibel (dB) is a non-specific unit of luminance based on a logarithmic scale (one-tenth of a log unit).
5. **Differential light sensitivity** represents the degree by which the luminance of a target requires to exceed background luminance in order to be perceived by the eye. The visual field is therefore a three-dimensional representation of differential light sensitivity at different points.
6. **Visible threshold** is the luminance of a given stimulus (measured in asb or dB) at which it is perceived 50% of the time when presented statically. The threshold is determined by increasing the intensity of the stimulus by 0.1 log unit steps. The human eye needs about a 10% change in brightness to discern a difference between light stimuli. For example, at a background illumination of 0.1 asb, the eye can detect a light stimulus that is 0.01 asb brighter, while at a background illumination of 1000 asb the eye requires a light that is 100 asb brighter to detect a difference. The threshold sensitivity (differential light sensitivity) is highest at the fovea and decreases progressively towards the periphery. After the age of 20 years the sensitivity decreases by 1 dB per 10 years. For example, at age 20 years the sensitivity at the fovea is 35 dB, at age 30 years it will be 34 dB, and at age 70 years it will be 30 dB.

Types of perimetry

Perimetry involves evaluation of the visual field. Because of the subjective variability of patients' responses, efforts have been made to standardize the many aspects of testing in an endeavour to eliminate as many variables as possible. Nevertheless, when interpreting a visual field defect, it is important to take into account the patient's reliability.

1. **Kinetic** perimetry is a two-dimensional assessment of the boundary of the hill of vision. It involves the presentation of a moving stimulus of known luminance or intensity from a non-seeing area to a seeing area until it is

perceived. The stimulus is moved at a steady speed along various meridia (clock hours) and the point of perception is recorded on a chart. By joining these points along different meridians an isopter is plotted for that stimulus intensity. Using stimuli of different intensities a contour map of the visual field with several different isopters can be plotted. Kinetic perimetry can be performed by simple confrontation, the tangent screen, the Lister perimeter and the Goldmann perimeter.

2. **Static** perimetry is a more difficult concept to perceive but once grasped forms the basis of modern glaucoma assessment. It is a three-dimensional assessment of the height (differential light sensitivity) of a predetermined area of the hill of vision. Static perimetry involves the presentation of non-moving stimuli of varying luminance in the same position to obtain a vertical boundary of the visual field.
   a. ***Suprathreshold*** perimetry is used mainly for screening. It involves the presentation of visual stimuli at luminance levels above expected normal threshold values (suprathreshold) in various locations in the visual field. Detected targets indicate grossly normal visual function, whereas missed targets reflect areas of decreased visual sensitivity. Missed points can later be quantified (i.e. threshold measured). Selecting an appropriate suprathreshold intensity is important; if too high, subtle early defects may be missed, and if too low, close to threshold, a large number of normal individuals will miss stimuli.
   b. ***Threshold*** perimetry is used for detailed assessment of the hill of vision by plotting the threshold luminance value in various locations in the visual field and comparing the results with age-matched 'normal' values. In Humphrey perimetry (*see* below), the intensity of a stimulus is increased by 4 dB steps until threshold is crossed. Threshold is then redetermined by decreasing the intensity by 2 dB steps. Because threshold perimetry represents quantitative assessment it is the most accurate method of monitoring glaucomatous visual field defects.

Printouts

Printouts of a test contain geographic (i.e. grey scale) and numerical results. The latter generally includes the raw data (i.e. sensitivity in dB at each test location), the difference between the patient's results and that expected of a patient of similar age, and summary data (visual field indices). These indices include an assessment of diffuse field loss, localized defects and patient reliability.

Sources of error

The skill of the perimetrist in setting up the test, explaining the procedure to the patient, reassuring the patient and monitoring performance is fundamental to obtaining an accurate field. However, errors may still occur as a result of one or more of the following factors:

1. **Miosis** decreases threshold sensitivity in the peripheral field and increases variability in the central field in both normal and glaucomatous eyes. Pupils less than 3 mm in diameter should therefore be dilated prior to perimetry.
2. **Lens opacities** have a profound effect on the visual field, which is exaggerated by miosis.
3. **Uncorrected refractive error** can cause a significant decrease of central sensitivity. If a hypermetropic patient who usually wears contact lenses is tested wearing spectacles this will have the effect of magnifying and enlarging any scotomas as compared to contact lenses.
4. **Spectacles** can cause rim scotomas if small-aperture lenses are used or if incorrectly dispensed.
5. **Ptosis**, even if mild, can result in suppression of the superior visual field.
6. **Inadequate retinal adaptation** may also lead to error if perimetry is performed soon after ophthalmoscopy.

Humphrey perimetry

The Humphrey perimeter consists of a white bowl with a background luminance of 31.5 asb, the lower end of photopic illumination. Target luminance can be varied between 0.08 asb and 10,000 asb brighter than background, which equates to a decibel range of 51–0. Variation in stimulus intensity is achieved by altering target size or luminance. Stimulus size is set prior to the test; only luminance is altered while the test is in progress in order to determine the threshold level for each point tested in the visual field.

Programs

The Humphrey has a range of suprathreshold and full threshold strategies (e.g. 30–1, 24–2). The number before the dash (24– or 30–) indicates the area of the tested field, in degrees from fixation. The 24° strategy tests 54 points and the 30° tests 76 points. The number after the dash (–1 or –2) describes the pattern of the points tested. The –2 strategy involves a grid of test points spaced 6° apart, offset from the vertical and horizontal meridia whereas the –1 includes points along the vertical and horizontal meridia. The most commonly performed central full threshold strategy is 24–2. Initially four points are tested to determine threshold levels, which are then used as a starting level for neighbouring points and so on until the entire field has been tested. Points where the anticipated response is outside 5 dB of that expected are retested a second time; the second response is indicated in brackets on the final printout. Different programs provided by the manufacturer include STATPAC, FASTPAC and SITA (Swedish Interactive Threshold Algorithm). The latter is the fastest and perhaps the most user-friendly. It also has the advantage of reacting to the patient's responses and timing to customize the determination of thresholds and the pacing of the test.

Reliability indices

Reliability indices (Fig. 9.41a) reflect the extent to which the patient's results are reliable and should be analysed first. If grossly unreliable, further evaluation of a visual field printout is pointless.

Fig. 9.41
Humphrey perimetric printouts (*see text*)

1. **Fixation losses** indicate steadiness of gaze during the test. They are detected by presenting stimuli in the physiological blind spot. If the patient responds, a fixation loss is recorded. The lower the number of losses the more reliable the test. A high fixation loss score may occur if the instrument has incorrectly plotted the blind spot.
2. **False positives** are detected when a stimulus is accompanied by a sound. If the sound alone is presented (without an accompanying light stimulus) and the patient still responds, a false positive is recorded. A high false positive score suggests a 'trigger-happy' patient and is the most sensitive indicator of an unreliable field.
3. **False negatives** are detected by presenting a stimulus much brighter than threshold at a location where sensitivity has already been recorded. If the patient fails to respond a false negative is recorded. A high false negative score indicates inattention. It may also be due to short-term fluctuation that is associated with glaucoma, and may be an indicator of disease severity rather than patient unreliability.

> *NB:* In patients who constantly fail to achieve good reliability indices it may be useful to switch to a suprathreshold strategy.

Displays

1. **The greyscale** (Fig. 9.41c), in which decreasing sensitivity is represented by darker tones, is the simplest to interpret. The scale at the bottom of the chart shows corresponding values of the greytone symbols in abs and dB. Each change in greyscale tone is equivalent to 5 dB change in threshold.
2. **The numerical** display (Fig. 9.41b) gives the threshold (dB) for all points checked. The figures in brackets indicate threshold at the same point checked a second time, if on initial testing it was at least 5 dB less sensitive than expected.
3. **The total deviation** represents the deviation of the patient's result from that of age-matched controls. The upper numerical display (Fig. 9.41d) illustrates the differences in dB and the lower display (Fig. 9.41f) exhibits these differences as grey symbols.
4. **Pattern deviation** (Figs 9.41e and g) is similar to total deviation except that it is adjusted for any generalized depression in the overall field which might be caused by other factors such as lens opacities or miosis.

Probability values (p) (Fig. 9.41h) indicating the significance of the defects are shown as <5%, <2%, <1% and <0.5%. The lower the p value the greater its clinical significance and the lesser the likelihood of the defect having occurred 'by chance'.

Global indices

Global indices (Fig. 9.41i) summarize the results in a single number and are principally used to monitor progression of glaucomatous damage rather than for initial diagnosis.

1. **Mean deviation** (MD) (elevation or depression) is a measure of the overall field loss.
2. **Pattern standard deviation** (PSD) is a measure of focal loss or variability within the field taking into account any generalized depression in the hill of vision. An increased PSD is therefore a more specific indicator of glaucomatous damage than MD.
3. **Short-term fluctuation** (SF) is an indication of the consistency of responses. It is assessed by measuring threshold twice at ten pre-selected points and is calculated on the difference between the first and second measurements.
4. **Corrected pattern standard deviation** (CPSD) is a measure of variability within the field after correcting for short-term fluctuation (intra-test variability).

Minimal criteria for glaucomatous damage

One of the following:

1. Glaucoma hemifield test outside normal limits on at least two consecutive occasions. This provides information concerning differences between the superior and inferior halves of the visual field by evaluating threshold at mirror image points above and below the horizontal meridian.
2. A cluster of three or more non-edge points in a location typical for glaucoma, all of which are depressed on PSD at a $p < 5\%$ level and one of which is depressed at a $p < 1\%$ level, on two consecutive occasions.
3. A CPSD that occurs in less than 5% of normal individuals on two consecutive fields.

> ***NB:*** Visual fields should not be interpreted in isolation but in conjunction with clinical findings such as the level of IOP, and the appearance of the optic disc and retinal nerve fibre layer.

Glaucomatous damage

Characteristic defects

1. The earliest changes suggestive of glaucoma consist of increased variability of responses in areas that subsequently develop defects. Alternatively there may be slight asymmetry between the two eyes.

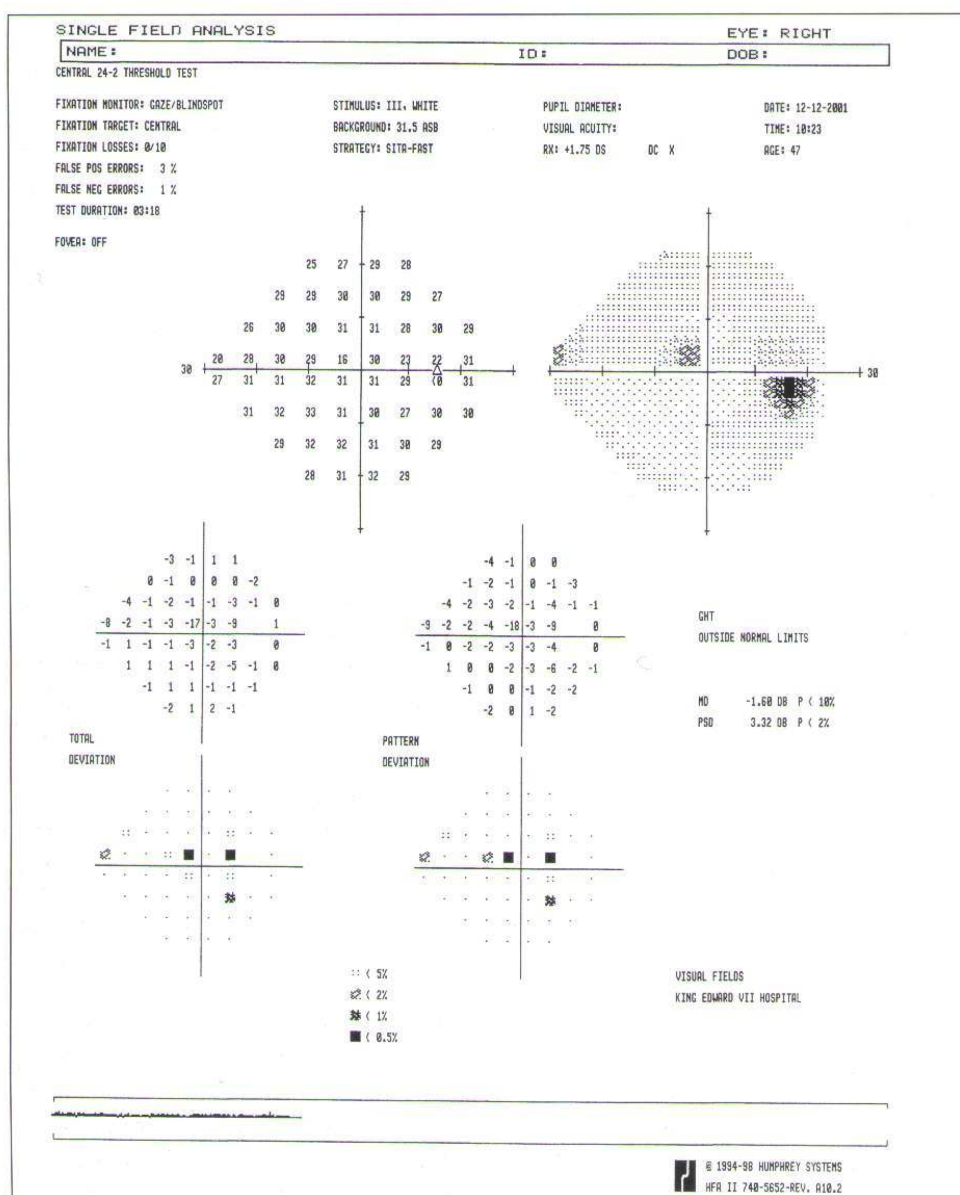


Fig. 9.42
Paracentral scotoma

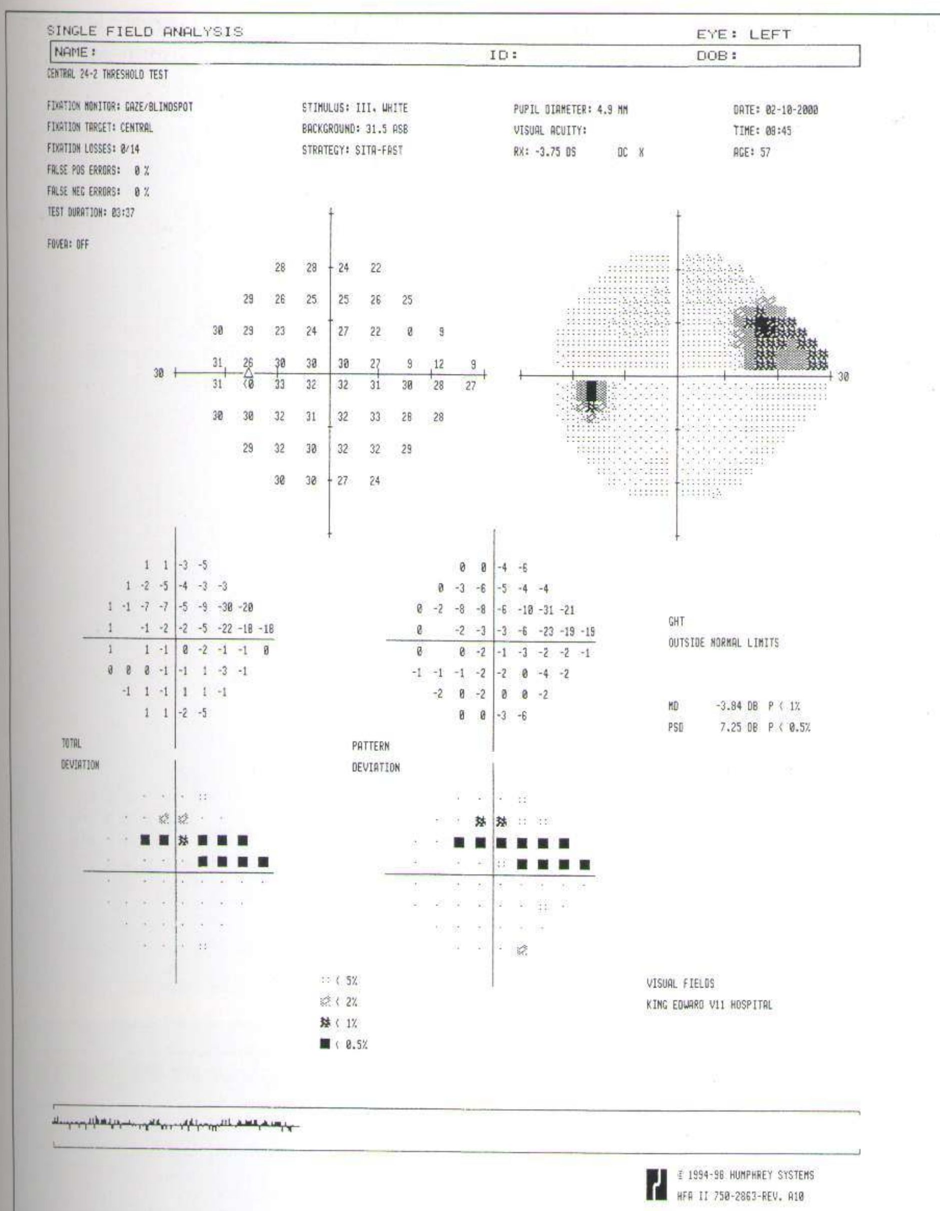


Fig. 9.43
Nasal (Roenne) step

2. Paracentral, small, relatively steep depressions, most commonly superonasally (Fig. 9.42), constitute approximately 70% of all early glaucomatous field defects. Since the defects respect the distribution of the retinal nerve fibre layer they terminate at the horizontal midline. Defects above and below the horizontal therefore are not aligned with each other.
3. A nasal (Roenne) step represents a difference in sensitivity above and below the horizontal midline in the nasal field (Fig. 9.43). It is a common finding usually associated with other defects. A temporal wedge is less common but has similar implications.
4. Arcuate-shaped defects develop as a result of coalescence of paracentral scotomas. They typically develop between 10° and 20° of fixation in areas that constitute downward, or more commonly, upward extensions from the blind spot around fixation (Bjerrum area). With time, they tend to elongate circumferentially along the distribution of arcuate nerve fibres (Seidel scotoma) and may eventually connect with the blind spot (arcuate scotoma), reaching to within 5° of fixation nasally (Fig. 9.44).
5. Enlargement and deepening of existing scotomas (Fig. 9.45) and development of fresh scotomas (Fig. 9.46).
6. Peripheral breakthrough due to damage to adjacent fibres.
7. A ring scotoma develops when arcuate defects in upper and lower halves of the visual field join. Misalignment between the two often preserves the nasal step (Fig. 9.47).
8. End-stage changes are characterized by a small island of central vision and an accompanying temporal island. The temporal island is usually extinguished before the central.

> ***NB:*** Progression of damage can be identified not only by increase in the number of scotomas and/or an increase in depth of existing scotomas but also by deterioration of total and pattern deviations and global indices (Fig. 9.48).

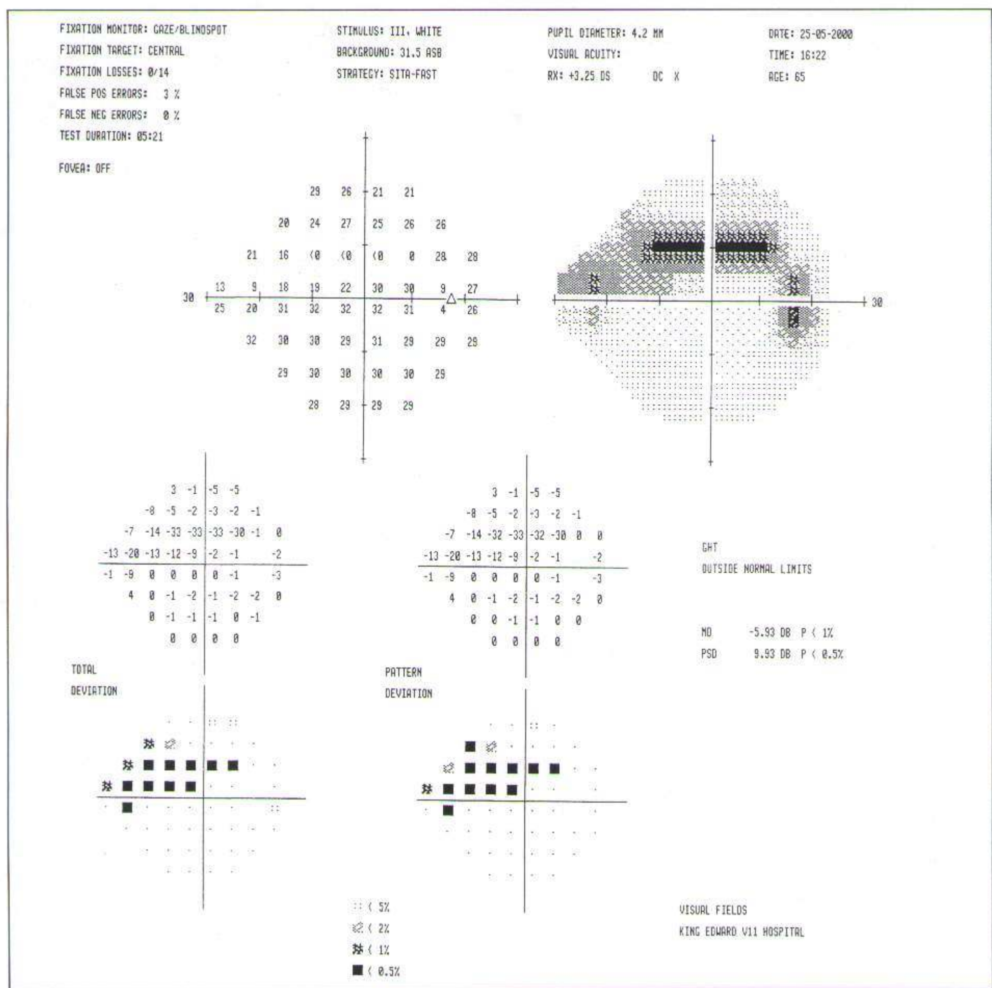


Fig. 9.44
Arcuate scotoma

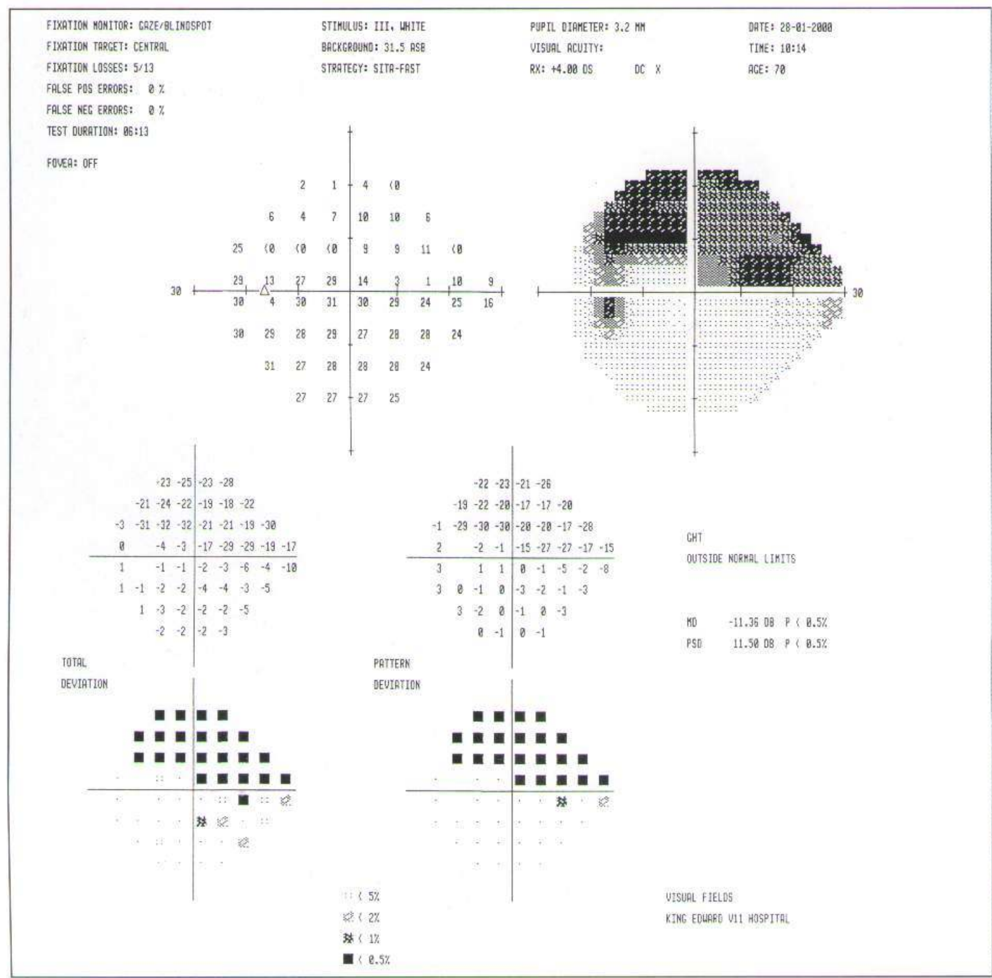


Fig. 9.45
Advanced superior arcuate visual field defect

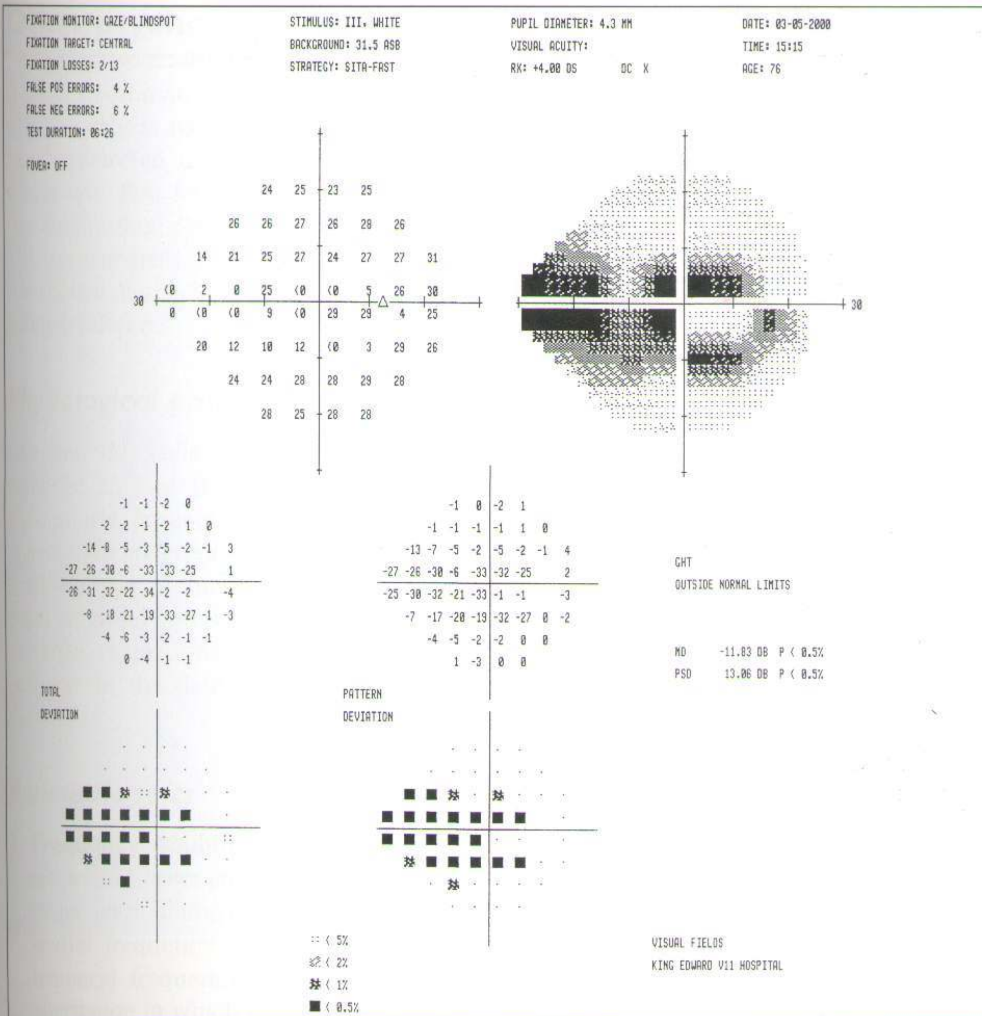


Fig. 9.46
Inferior and superior arcuate visual field defects

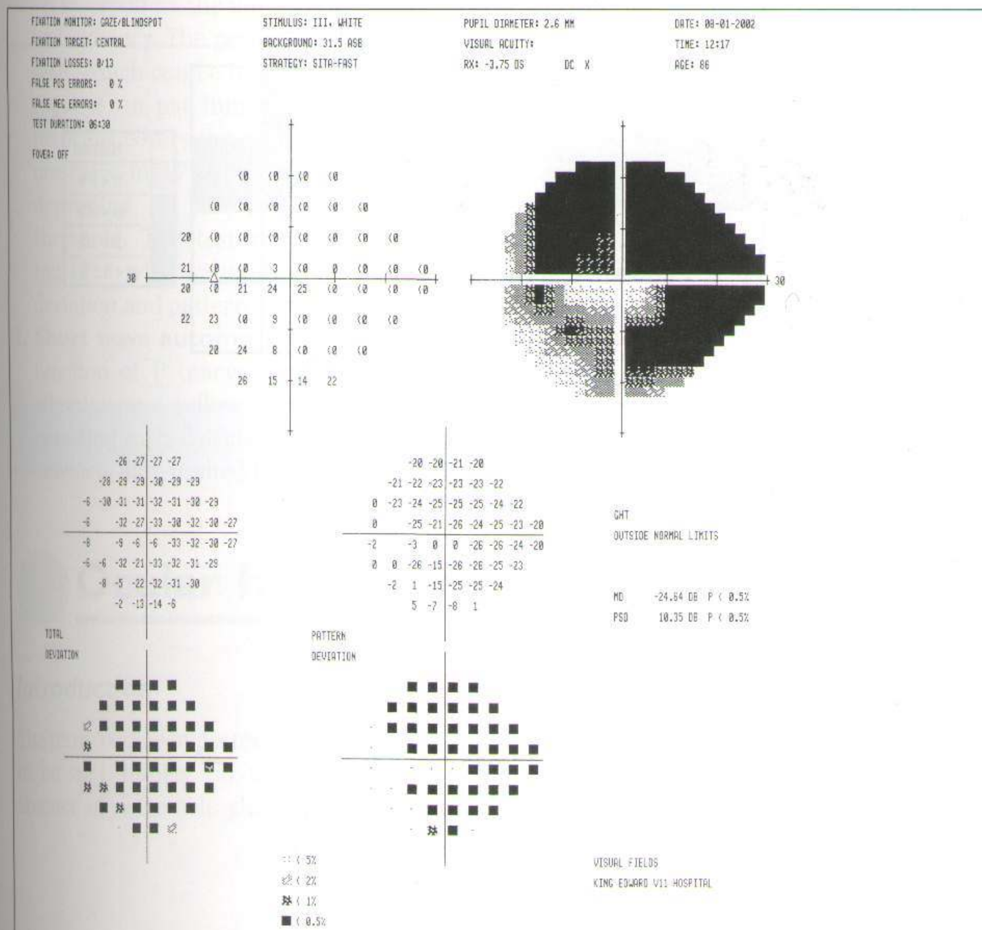


Fig. 9.47
Advanced visual field loss

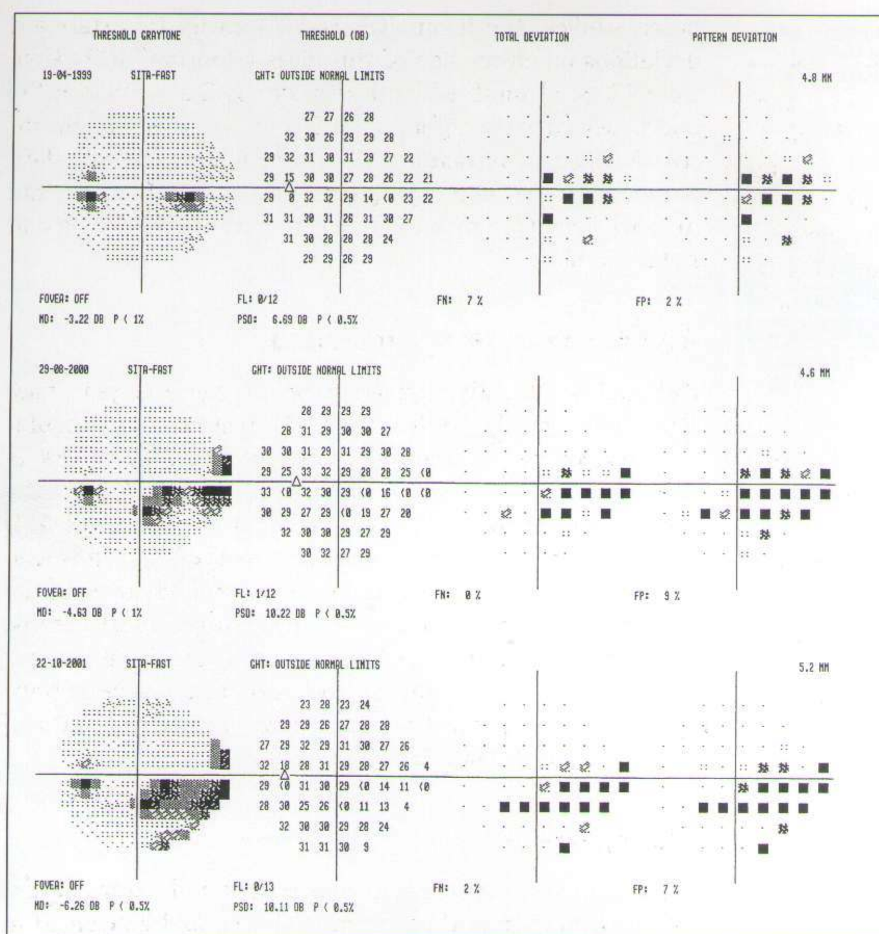


Fig. 9.48
Progression of visual field defects over three years

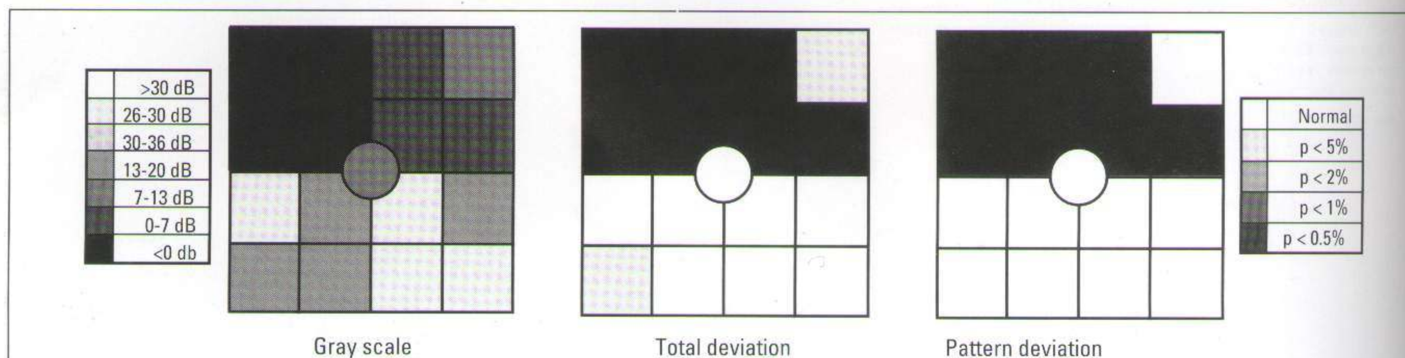


Fig. 9.49
Printout of frequency doubling perimetry showing moderate visual field loss

Other psychophysiological tests

It has been estimated that focal loss of at least 20% of retinal ganglion cells is required before glaucomatous field defects can be detected using conventional perimetry. Learning effects are often found whereby field defects disappear on repeated testing. Genuine early glaucomatous defects may also be transient and disappear with lowering of IOP. Alternative methods of detecting early defects are therefore being developed.

Physiological principles

Ganglion (M) cells with relatively large-diameter axons comprise 25% of the ganglion cell population. They are particularly susceptible to glaucomatous damage and appear to be preferentially lost in early glaucoma. A loss of a small number of these cells therefore has a considerable effect on visual function. Psychophysiological tests designed to target visual function provided by this magnocellular pathway in the detection of early glaucoma have been devised.

Perimetric tests

1. **Frequency doubling perimetry** is a simple and rapid test which shows considerable promise. It is based on the frequency doubling illusion which is produced when a low spatial frequency sinusoidal grating undergoes high temporal frequency counter phase flicker. The rapid alternation in which the light bars become dark and vice versa, produces the illusion of the grating having doubled its frequency. The perimeter is a tabletop portable instrument which can be used under normal room lighting and requires no patching, since the viewing canopy automatically covers the eye not being tested. The stimuli are presented in 17 or 19 sectors in the central 20° or 30° depending on the program used, screening or full threshold. The test results are displayed and printed together with reliability indices, probabilities, mean deviation and pattern standard deviation (Fig. 9.49).
2. **Short wave automated perimetry** (SWAP) reflects the function of P (parvocellular) cells by displaying a blue stimulus on a yellow background. It is a good method of detecting early defects in young patients but lens-induced artefacts have limited its use in elderly patients.

Ocular hypertension

Introduction

The term 'ocular hypertension' is used when the IOP is found to be >21 mmHg on two consecutive occasions, in the absence of detectable glaucomatous damage. In population based studies, the mean IOP is 16 mmHg; two standard deviations on either side of this gives a 'normal' IOP range from 11 to 21 mmHg. The distribution is Gaussian with the curve skewed to the right (Fig. 9.50). In the elderly the mean IOP is higher, particularly in women, and the standard deviation greater than in younger individuals. This means that 'normal' IOP in elderly women may range up to 24 mmHg and not 21 mmHg.

Risk for developing glaucoma

Although 4–7% of the population over the age of 40 years have IOPs >21 mmHg, only 1% of individuals with ocular hypertension will develop glaucoma each year. The risk of damage increases as the IOP rises. The prevalence of primary open-angle glaucoma (POAG) in relation to screening IOP is shown in Table 9.1. There is no infallible way of predicting who will eventually develop glaucoma. Structural changes in the retinal nerve fibre layer and the optic nerve head precede changes in visual function (pre-perimetric glaucoma). It may therefore take up to several years before damage can be detected by conventional perimetry, which necessitates loss of 20% of the ganglion cell population.

Management

Most patients with ocular hypertension do not require treatment and only those at high risk should be treated in

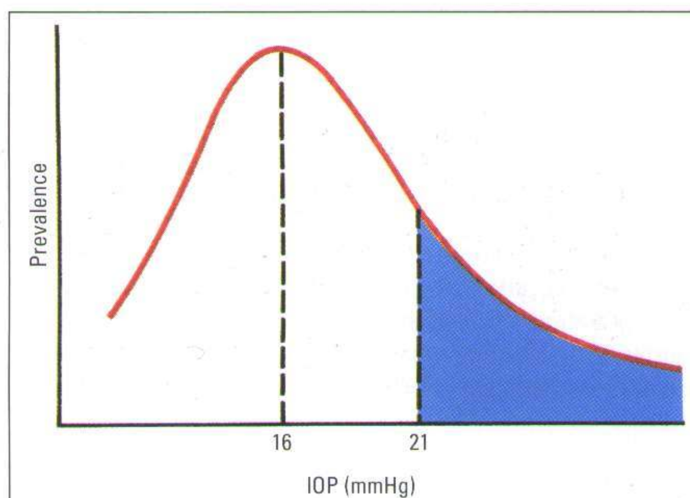


Fig. 9.50
Distribution of intraocular pressure in the general population

Table 9.1 Relationship between prevalence of POAG and IOP

IOP (mmHg)	*Prevalence of POAG (%)*
16–21	1.5
22–29	8
30 or over	25

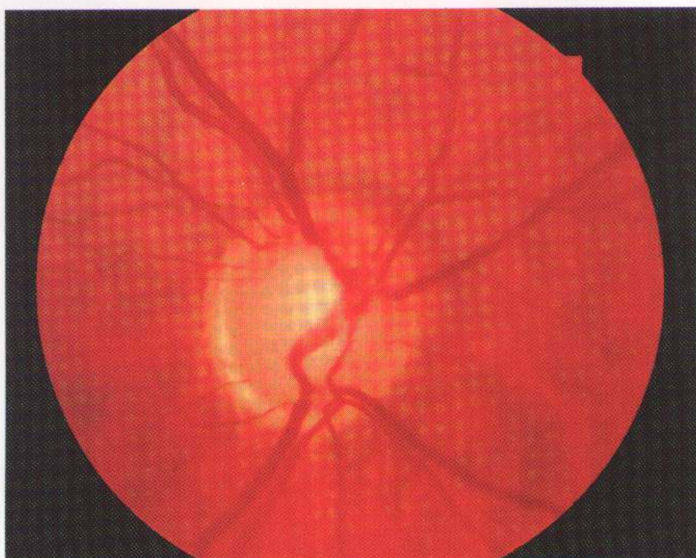


Fig. 9.51
Vertical cup–disc ratio over 0.7

order to delay or prevent the development of POAG. It should be remembered that once treatment is instituted, it is continued throughout the patient's lifetime and may have significant side effects. Therapeutic decisions in individual patients are based on a combination of risk factors as follows:

1. High risk factors

- Retinal nerve fibre layer defects.
- Parapapillary changes.
- IOP 30 mmHg or more.
- IOP 26 mmHg or more and central corneal thickness < 555 μm.
- Vertical cup–disc ratio 0.4 or more and corneal thickness < 588 μm.

Most patients with high risk factors should be treated because treatment is effective in delaying or preventing the development of POAG in a significant proportion of cases. A change of IOP is more important than a specific level and it is reasonable to aim for a 20% reduction of IOP.

2. Moderate risk factors

- IOP of 24–29 mmHg without nerve fibre layer defects.
- Vertical cup–disc ratio > 0.3 (Fig. 9.51) and central corneal thickness > 588 μm.
- Family history of POAG in a first degree relative.
- High myopia.

In these patients annual examination of the optic discs and perimetry is appropriate. Treatment is withheld until damage is documented.

Primary open-angle glaucoma

Introduction

Primary open-angle glaucoma (POAG), also referred to as chronic simple glaucoma, is a generally bilateral, but not always symmetrical disease, characterized by:

- Adult onset.
- An IOP > 21 mmHg at some point in the course of the disease.
- An open angle of normal appearance.
- Glaucomatous optic nerve head damage.
- Visual field loss.

Despite this definition it should be emphasized that approximately 16% of all patients with otherwise characteristic POAG will have IOPs consistently below 22 mmHg. Moreover, the majority of individuals with IOP > 21 mmHg do not have glaucoma. POAG is the most prevalent type of glaucoma, affecting approximately 1 in 100 of the general population over the age of 40 years. It affects both sexes equally and is responsible for about 12% of all cases of blind registration in the UK and the USA.

Risk factors and associations

1. **Age**. POAG is more common in older individuals, most cases presenting after the age of 65 years. It is unusual for this diagnosis to be made before the age of 40 years.
2. **Race**. POAG is significantly more common, develops earlier, and is more severe, in black people than in white.
3. **Family history and inheritance**. POAG is frequently inherited, probably in a multifactorial manner. The responsible genes are thought to show incomplete penetrance and variable expressivity. Intraocular pressure, facility of aqueous outflow and optic disc size are also genetically determined. First-degree relatives of patients with POAG are at increased risk of developing POAG; however, estimates of exact risk are lacking because the disease develops in older individuals and long-term follow-up is required for accurate figures. However, an approximate risk to siblings of 10% and to offspring of 4%, has been suggested.
4. **Myopia** is associated with an increased incidence of POAG and myopic eyes are also more susceptible to pressure-induced damage.
5. **Retinal disease**. Central retinal vein occlusion is associated with an increased incidence of POAG. Approximately 5% of patients with rhegmatogenous retinal detachment and 3% of those with retinitis pigmentosa have associated POAG.

Steroid responsiveness

The normal population can be divided into three groups on the basis of their IOP response to a 6-week course of topical betamethasone.

1. **High responders** exhibit a marked elevation of IOP (>30 mmHg).
2. **Moderate responders** display a moderate elevation of IOP (22–30 mmHg).
3. **Non-responders** manifest virtually no change in IOP.

The incidence of steroid responders is shown in Table 9.2. Topical steroids should be used with caution in these individuals. However, in a high or intermediate steroid responder, the 'strong' steroids (dexamethasone, betamethasone and prednisolone) are equipotent in their ability to raise IOP, while fluorometholone has a lesser propensity to raise IOP; fluorometholone raises IOP half as much as betamethasone.

Table 9.2 Incidence of steroid responsiveness

	High (%)	*Moderate (%)*	*Non (%)*
General population	5	35	60
Patients with POAG	90	10	0
Siblings of patients with POAG	30	50	20
Offspring of patients with POAG	25	70	5

NB: Systemic steroids are much less prone to cause elevation of IOP, but more likely to induce cataract.

Genetics

1. **Steroid responsiveness** is of great interest in the genetics of POAG. A mutation of the *MYOC* gene is strongly associated with a subset of juvenile open-angle glaucoma, and is present in about 4% of adults with POAG. The gene was previously named *TIGR* (trabecular induced glucocorticoid response). It resides in the *GLCIA* region of the long arm of chromosome 1 and codes for a protein called myocilin. The administration of steroids in steroid responders induces gene expression and the production of excessive quantities of myocilin. However, the exact role of myocilin in the pathogenesis of steroid-induced elevation of IOP is currently unclear.
2. **Other aspects**. All gene loci associated with POAG have a prefix GLC1, with a suffix letter indicating the temporal order in which the gene is identified. Genes that have so far been identified in certain families with POAG lie on chromosome 2 (*GLC1B*), chromosome 3 (*GLC1C*), chromosome 8 (*GLC1D*), chromosome 10 (*GLC1E*) and chromosome 7 (*GLC1F*).

Pathogenesis of glaucomatous damage

Elevation of IOP in POAG is caused by increased resistance to aqueous outflow in the trabecular meshwork. Retinal ganglion cell death occurs predominantly through apoptosis (programmed cell death) rather than necrosis. The preterminal event is Ca^{++} influx into the cell body and an increase in intracellular nitric oxide. Glutamine metabolism has a profound effect on this process. The factors that influence the rate of cell death are multiple, but current opinion is polarized between ischaemic and mechanical aetiologies of damage.

1. **The ischaemic theory** postulates that compromise of the microvasculature with resultant ischaemia in the optic nerve head is responsible.
2. **The direct mechanical theory** suggests that raised IOP directly damages the retinal nerve fibres as they pass through the lamina cribrosa. It is likely that the pressure gradient around the optic nerve head rather than the absolute IOP is relevant in this context.

Screening

Population screening with tonometry alone is unsatisfactory, since it will label as 'normal' a significant number of cases with other features of POAG such as cupping and visual field loss. Even with the additional criterion of a vertical cup–disc ratio of >0.4, only 60% of potential POAG patients will be

identified. Until more accurate methods of mass screening are available, screening should therefore include visual field examination, tonometry and ophthalmoscopy. Individuals with a family history of glaucoma in first-degree relatives should be screened from the age of 40 years. Provided initial assessment is normal, subsequent review should be at 2-yearly intervals until the age of 50 years and then annually thereafter.

Clinical features

Symptoms

POAG is asymptomatic until significant loss of visual field has occurred. This is because damage occurs gradually and fixation is involved late in the course of the disease. Although the disease is almost invariably bilateral, progression is often asymmetrical. Patients therefore frequently present with significant visual field loss in one eye and less advanced disease in the other. Even highly self-analytical individuals may be unaware of large areas of visual field loss although occasionally early defects may be discovered by chance.

Signs

1. **Raised IOP**. This objective measurement has proved both a stumbling block and a great benefit in the diagnosis of POAG. Approximately 2% of the general population over the age of 40 years have IOPs > 24 mmHg and 7% have IOPs > 21 mmHg. However, only about 1% of these have glaucomatous visual field loss. This issue is further complicated by patients with 'normal' IOP (<22 mmHg) who develop glaucomatous visual field loss and cupping.
2. **Diurnal fluctuations in IOP** of up to 5 mmHg occur in approximately 30% of normals. In POAG this fluctuation is exaggerated and occurs in about 90% of cases. For this reason, a single pressure reading of 21 mmHg or less does not necessarily exclude the diagnosis of POAG, nor should a single reading of >21 mmHg do more than arouse suspicion. In order to detect fluctuations of IOP, it may be necessary to measure the IOP at different times during the day (phasing). Asymmetry of the IOP between the two eyes of 5 mmHg or more should arouse suspicion, since irrespective of the absolute value the eye with the higher reading may be abnormal.
3. **Optic disc changes**. POAG is often diagnosed after finding suspicious optic or asymmetrical discs on routine examination.
4. **Visual fields** show typical changes as previously described.
5. **Gonioscopy** shows a normal open angle.

Management

The primary aim of treatment is to prevent functional impairment of vision within the patient's lifetime by slowing the rate of ganglion cell loss closer to that of the normal population (approximately 5000/year). Currently the best method of achieving this goal is the lowering of IOP. Other modalities aimed at inhibition of ganglion cell apoptosis are currently under evaluation.

Baseline evaluation

Clear and concise records of baseline parameters are essential to monitor future progress.

1. **Visual acuity** and **refractive state**.
2. **Slit-lamp biomicroscopy**, paying attention to signs of secondary glaucomas which may masquerade as POAG.
3. **Applanation tonometry**, noting the time of day.
4. **Gonioscopy** should automatically follow applanation tonometry. However, if a coupling substance is required, gonioscopy should be delayed until the optic discs and visual fields have been assessed.
5. **Ophthalmoscopy** should be performed and the appearance of the disc documented by drawing and if possible also by photography.
6. **Perimetry**. The type of perimetry depends on the instrumentation available, the patient's age and visual acuity. In patients with significant lens opacities, perimetry should be performed with dilated pupils.

Patient instruction

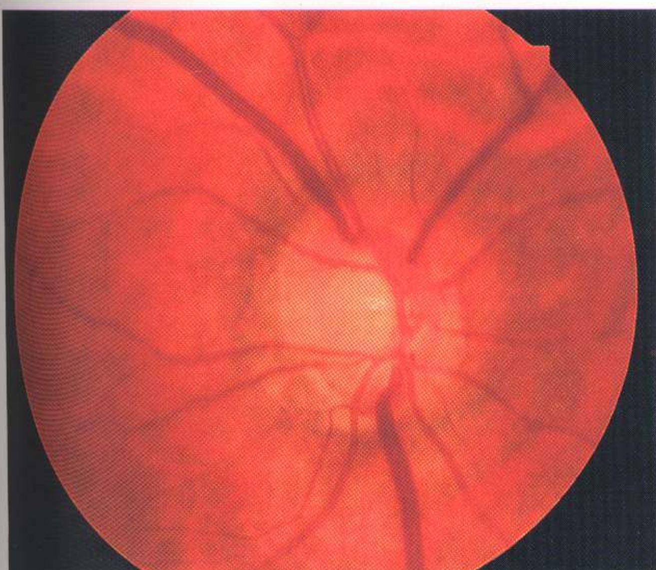
A simple explanation should be offered concerning the nature of the disease and an explanatory booklet provided. The patient should be taught how to instil drops and the intervals between medications should be specified. At follow-up visits the patient's proficiency at instilling drops should be checked. In order to minimize systemic absorption the patient should be instructed either to perform lacrimal sac occlusion (by applying pressure at the medial canthus) or to close the eyes for about 3 minutes after instillation. Potential adverse effects should be explained and subsequently asked for at follow-up visits.

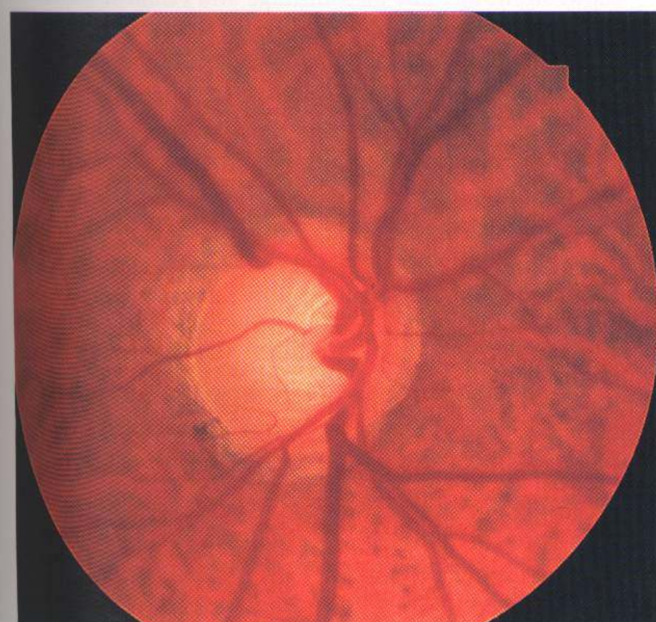
Grading of glaucomatous damage

1. **Mild damage** is characterized by early visual field defects (MD < –6 dB) (*see* Fig. 9.42) and mild cupping (Fig. 9.52).
2. **Moderate damage** is characterized by a definite arcuate scotoma (MD < –12 dB) (*see* Fig. 9.44) and moderate thinning of neuroretinal rim (Fig. 9.53).
3. **Severe damage** is characterized by extensive visual field loss (MD > –12 dB) (*see* Fig. 9.47) and marked cupping (Fig. 9.54).
4. **End-stage disease** is characterized by a small residual field and minimal residual neuroretinal rim (Fig. 9.55).

Treatment goals

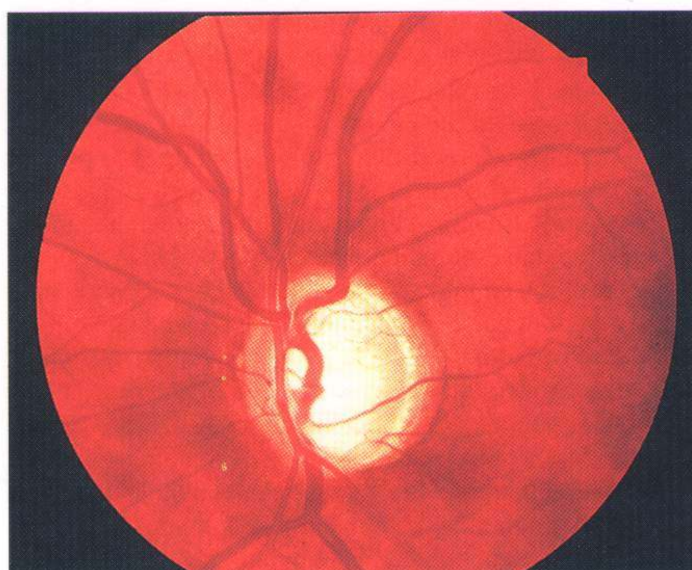
1. **Target pressure**. It is assumed that the pre-treatment level of IOP has damaged the optic nerve and will continue to do so. An IOP level is identified below which further damage is considered unlikely (target pressure). The target

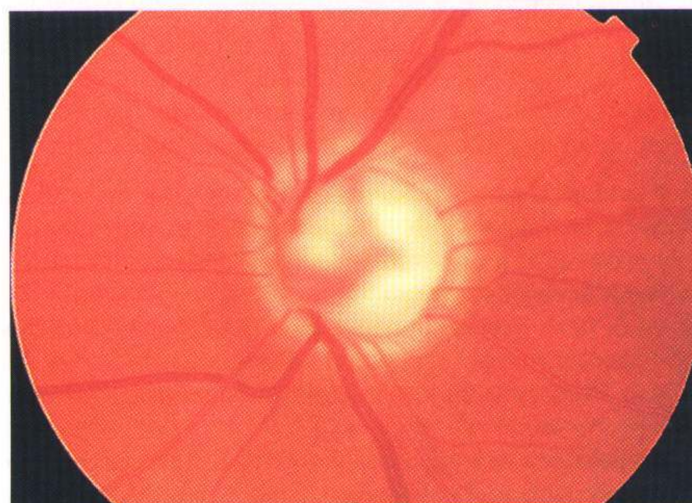

Fig. 9.52
Mild glaucomatous cupping


Fig. 9.53
Moderate glaucomatous cupping

pressure is identified taking into account the severity of existing damage, the level of IOP, the rapidity with which damage occurred (if that is known), as well as the age and general health of the patient. Therapy should maintain the IOP at or below the target level.

2. **Monitoring** is performed of the optic nerve and visual fields. In the event of further damage the target IOP is reset at a lower level. Although there is no 'safe' level, progression is uncommon if the IOP is <16 mmHg. As the disease progresses the degree of redundancy or 'reserve capacity' within the visual system diminishes and the loss of each remaining ganglion cell inflicts a greater impact on visual function. Lower target pressures are therefore required in patients with advanced disease.


Fig. 9.54
Advanced glaucomatous cupping


Fig. 9.55
Total glaucomatous cupping

Medical therapy

1. **Basic principles**
   - Any chosen drug should be used in its lowest concentration and as infrequently as possible consistent with the desired therapeutic effect.
   - Ideally the drug with the fewest potential side effects should be used.
   - Initial treatment is usually with one drug.
2. **Follow-up** should be after 4 weeks.
   - A fall in IOP of >4 mmHg is considered significant (i.e. caused by the drug as opposed to chance fluctuation) but may not always be sufficient (depending on treatment goals).
   - If the response is satisfactory subsequent assessment is after 1 month and at 3 or 4-monthly intervals thereafter.
   - If the response is unsatisfactory the initial drug is withdrawn and another substituted.

- If the response is still unsatisfactory yet another drug is added or a combined preparation (i.e. timolol–latanoprost or timolol–dorzolamide) substituted. When two separate drugs are used the patient should be instructed to wait 5 minutes before instilling the second drug to prevent washout of the first drug.

3. **Perimetry**. If control is good and the appearance of the optic disc stable, annual perimetry is sufficient.
4. **Gonioscopy** should also be performed annually because the anterior chamber gradually shallows with age.
5. **Causes of failure**
   - Inappropriate target pressure. If the IOP runs in the upper part of the statistically normal range, progressive field loss is common.
   - Non-compliance with therapy occurs in at least 25% of patients.
   - Wide fluctuations in IOP frequently occur in patients treated medically.

Laser trabeculoplasty

In this procedure discrete argon or diode laser burns are applied to the trabeculum to enhance aqueous outflow and lower IOP. The therapeutic effect is often transient, lasting a few years, so that laser therapy may merely defer the need for filtration surgery. The following are the main indications:

1. **Avoidance of polypharmacy**, usually with more than two preparations. In this situation laser therapy may be considered as a substitute for another drug.
2. **Avoidance of surgery**
   - In elderly patients in whom laser therapy may defer the need for surgery to beyond life expectancy.
   - In black patients in whom filtration surgery carries a poorer prognosis.
3. **As primary therapy** in patients who are expected not to comply with medical therapy. Since IOP reduction with laser is seldom greater than 30%, an IOP > 28 mmHg is unlikely to be adequately controlled by laser alone.
4. **Patients non-compliant with medical therapy**.

Trabeculectomy

This involves the surgical creation of a fistula between the angle of the anterior chamber and the sub-Tenon space, which allows egress of aqueous from the anterior chamber into a 'drainage bleb' under the upper eyelid. Progressive damage is less likely after trabeculectomy than with medical therapy because the resultant IOP is often significantly lower and less likely to fluctuate. The timing of surgery depends on the amount of visual loss that has occurred, the rapidity of deterioration and life expectancy. The following are the main indications:

1. **Failed medical therapy** and/or **laser trabeculoplasty**.
2. **Unsuitability** for laser therapy due to poor patient cooperation or inadequate visualization of the trabeculum (narrow angle, corneal opacification).
3. **Advanced disease** requiring a very low target pressure may benefit from early surgery.

> *NB:* Some ophthalmologists in the UK would consider trabeculectomy when a single topical medication fails to achieve the target pressure or prevent progressive optic nerve damage.

Normal-tension glaucoma

Definition

Normal-tension glaucoma (NTG), also referred to as low-tension glaucoma, is a variant of POAG. Predominantly a disease of the elderly, it is more common in females. It is characterized by:

- A mean IOP equal to or less than 21 mmHg on diurnal testing.
- Glaucomatous optic disc damage and visual field loss.
- Open drainage angle on gonioscopy.
- Absence of secondary causes for glaucomatous optic disc damage.

> *NB:* The classification of POAG into two types (i.e. normal-tension and high-tension) is based on an epidemiologically derived normal IOP. It is therefore essentially an arbitrary division and may not have significant clinical value. The prevalence of NTG in individuals over the age of 40 years is 0.2% and the condition accounts for 16% of all cases of POAG.

Signs

1. **The IOP** is usually in the high teens, but may rarely be in the low teens. In asymmetrical disease the more damaged disc corresponds to the eye with the higher IOP.
2. **Optic nerve head**
   - Both glaucomatous cupping or parapapillary changes are identical to those seen in POAG.

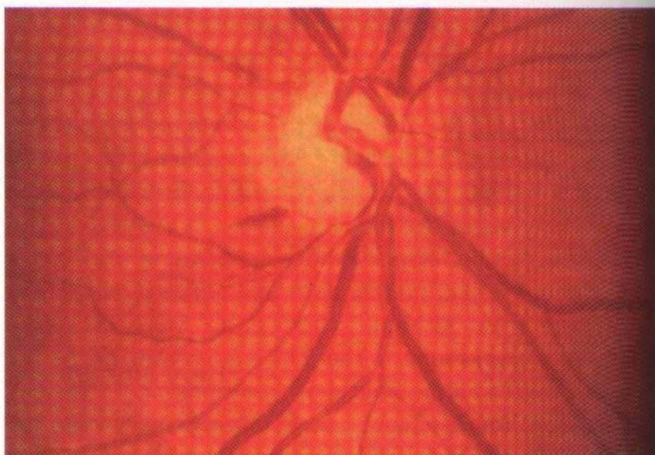


Fig. 9.56
Moderate glaucomatous cupping with a splinter haemorrhage

- Splinter haemorrhages at the disc margin (Fig. 9.56) are more frequent in NTG and may indicate progressive damage of the retinal nerve fibre layer.
- Acquired optic disc pits characterized by localized excavations of the lamina cribrosa are also more frequent.

3. **Visual field defects** are essentially the same as in POAG although it has been suggested that in NTG they tend to be closer to fixation, deeper, steeper and more localized. In some patients, even without treatment, field changes are non-progressive. However, because of frequent delay in diagnosis, patients with NTG tend to present with more advanced damage than those with POAG. Patients with unilateral field defects have a 40% chance of developing field loss in the fellow eye within 5 years.
4. **Other characteristics** which are more common in NTG than in POAG include:
   - Peripheral vascular spasm on cooling (Raynaud phenomenon).
   - Migraine may be more common, although this has not been confirmed in a population-based survey.
   - Nocturnal systemic hypotension and overtreated systemic hypertension.
   - Reduced blood flow velocity in the ophthalmic artery when measured with transcranial Doppler ultrasonography.
   - Paraproteinaemia and the presence of serum autoantibodies.

Treatment

This is indicated only in patients with documented progressive visual field loss. The aim is to reduce the IOP by at least 30%.

1. **Medical** treatment. Betaxolol may be the drug of choice because of its beneficial effects on optic nerve blood flow in addition to its IOP-lowering properties. However, prostaglandin analogues tend to have a greater ocular hypotensive effect in eyes with normal IOP.
2. **Trabeculectomy** should be considered, in at least one eye, if progressive field loss occurs despite IOP in the lower teens.
3. **Systemic calcium channel blockers** (e.g. nifedipine) may be considered in younger patients and in those with early disease. Ideally, peripheral vasospasm should be confirmed by nailfold capilloscopy before commencing treatment. Long-term therapy is warranted only if visual fields remain stable after a short-term (2–3 months) therapeutic trial.
4. **Monitoring of systemic blood pressure** for 24 hours. If a significant nocturnal drop is detected, it may be necessary to avoid anti-hypertensive medication, especially if taken prior to bedtime.

Differential diagnosis

1. **POAG** presenting with normal IOP because of a wide diurnal fluctuation. This can be excluded by phasing (diurnal IOP curve) over an 8-hour period in order to detect a pressure spike of >21 mmHg.
2. **Congenital optic disc anomalies** such as large optic disc pits or colobomas may be mistaken for acquired glaucomatous cupping.



Primary angle-closure glaucoma

Introduction

Primary angle-closure glaucoma (PACG) is a condition in which elevation of IOP occurs as a result of obstruction of aqueous outflow by partial or complete closure of the angle by the peripheral iris. Unlike POAG, the diagnosis depends largely on examination of the anterior segment and careful gonioscopy. A normal optic nerve head and visual field do not preclude a diagnosis of PACG. This disease occurs in anatomically predisposed eyes and is frequently bilateral, although presentation of the acute form is often unilateral. Based on the mechanism of angle closure, two forms of PACG are recognized: (a) *pupillary block* and (b) *plateau iris syndrome*, which is rare.

Risk factors

1. **Age**. The average age at presentation is about 60 years; prevalence increases thereafter.
2. **Gender**. Females are more commonly affected than males by a ratio of 4:1.
3. **Race**. In caucasians the condition accounts for about 6% of all glaucomas and it affects approximately 1:1000 individuals over the age of 40 years. PACG is more common in South-East Asians, Chinese and Eskimos and is uncommon in black people.
4. **Family history**. First-degree relatives are at increased risk because predisposing anatomical factors are often inherited (*see* below).

Anatomical predisposing factors

1. **Relatively anterior location of the iris–lens diaphragm.**
2. **Shallow anterior chamber**.
3. **Narrow entrance to the chamber angle**.
   Proximity of the peripheral iris to the cornea facilitates angle closure. The following three interrelated factors are responsible for these characteristics:
   a. Lens size. The lens is the only ocular structure which continues to increase in size throughout life. Axial (anteroposterior) growth brings its anterior surface closer to the cornea, while equatorial growth slackens the suspensory ligament, allowing the iris–lens diaphragm to move anteriorly. Both these factors cause gradual and progressive shallowing of the anterior chamber. Eyes with PACG have shallower anterior chambers than normal eyes, and women have shallower anterior chambers than men.

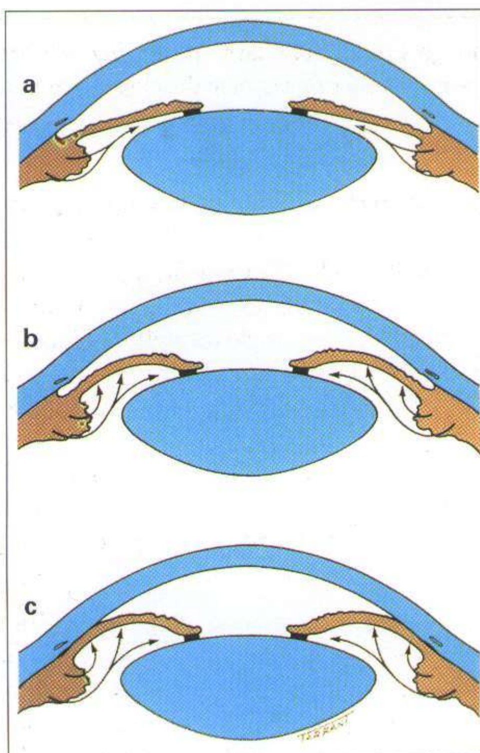


Fig. 9.57
Mechanism of angle closure. (**a**) Relative pupil block; (**b**) iris bombé; (**c**) iridocorneal contact

b. *Corneal diameter*. Anterior chamber depth and angle width are related to the corneal diameter. Eyes with PACG have corneal diameters 0.25 mm smaller than normal.

c. *Axial length*. The position of the lens and the corneal diameter are related to the axial length of the globe. A short eye, which is also frequently hypermetropic, has a small corneal diameter and a relatively anteriorly located lens. For this reason eyes with nanophthalmos are at increased risk of angle-closure glaucoma.

Pathogenesis

The pathogenesis of acute PACG is incompletely understood. Normally the pressure in the posterior chamber exceeds that in the anterior chamber due to a physiological degree of resistance at the pupil, since the iris rests posteriorly on the anterior lens capsule.

1. **The dilator muscle theory** postulates that contraction of the dilator pupillae exerts a posterior vector. This increases the amount of apposition between the iris and the anteriorly located lens, enhancing the degree of physiological pupil block (Fig. 9.57a). Simultaneous dilatation of the pupil renders the peripheral iris more flaccid. The pupil block causes the pressure in the posterior chamber to increase and the peripheral iris bows anteriorly (iris bombé) (Fig. 9.57b). Eventually the iris touches the posterior corneal surface, obstructing the angle and the IOP rises (Fig. 9.57c).
2. **The sphincter muscle** theory postulates that the sphincter pupillae is the prime culprit in precipitating angle closure. The pupillary blocking force of the sphincter is greatest when the diameter of the pupil is approximately 4 mm.

Classification

Although PACG can be divided into five overlapping stages the condition does not necessarily progress from one stage to the next in an orderly sequence. In practice, a combination of these clinical stages is often seen:

1. **Latent**.
2. **Subacute (intermittent)**.
3. **Acute congestive**.
4. **Postcongestive**.
5. **Chronic**.
6. **Absolute** is the end-stage of acute congestive PACG in which the eye is completely blind and will not be discussed further.

Latent angle-closure glaucoma

Clinical features

This is a retrospective diagnosis, only made with any degree of certainty in one eye during an attack of acute congestive glaucoma in the other. It can therefore often only be *suspected* prospectively. Essentially, the term 'latent angle closure' implies an anatomically predisposed eye.

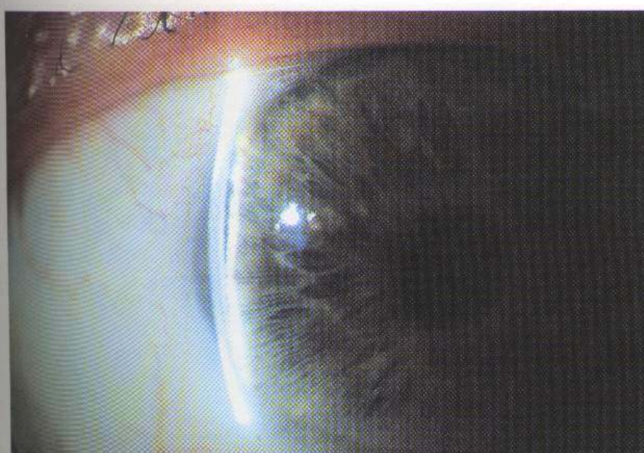
1. **Symptoms** are absent.
2. **Slit-lamp biomicroscopy**
   - Axial anterior chamber depth is less than normal.

> ***NB:*** This can also be demonstrated by shining a penlight across the eye from the temporal side. Due to the convexity of the iris–lens diaphragm, the nasal iris manifests a crescentic shadow, appearing dark relative to the temporal iris (the eclipse sign) (Fig. 9.58).



Fig. 9.58
'Eclipse' sign elicited by directing a light across the anterior chamber from the temporal side and noting a shadow on the nasal side (Courtesy of J. Salmon)


Fig. 9.59
Convex-shaped iris–lens diaphragm


Fig. 9.60
Close proximity of iris to the peripheral cornea

- Convex-shaped iris–lens diaphragm (Fig. 9.59).
- Close proximity of the iris to the cornea (Fig. 9.60).

3. **Gonioscopy** shows an 'occludable' angle in which the pigmented trabecular meshwork is not visible (Shaffer grade 1 or 0) without indentation or manipulation in at least three quadrants.
4. **The clinical course** without treatment may be as follows:
   - The IOP may remain normal.
   - Acute or subacute angle closure may develop.
   - Chronic angle closure may develop, without passing through subacute or acute stages.

Treatment

- If one eye has had acute or subacute PACG, the fellow eye should undergo prophylactic peripheral laser iridotomy because, without treatment, the risk of an acute pressure rise during the next 5 years is about 50%.
- If both eyes have latent PACG, no parameter or provocative test is sufficiently sensitive or accurate to determine whether acute PACG will later develop. However, since the risks of laser iridotomy are small, if carefully undertaken laser treatment may be considered.

> ***NB:*** Although prophylactic laser iridotomy will prevent an acute attack, 15% of eyes may develop a late rise in IOP.

Subacute angle-closure glaucoma

Subacute (intermittent) PACG occurs in a predisposed eye with an occludable angle in association with intermittent pupillary block. Rapid closure of the angle results in sudden increase in IOP. The pupillary block is then spontaneously relieved, the angle opens and the IOP returns to normal. Attacks may be precipitated by physiological mydriasis (watching television in a dark room), or by physiological shallowing of the anterior chamber when the patient assumes a prone or semiprone position (when sewing or reading). Emotional stress may occasionally be a precipitating factor.

1. **Diagnosis** is based on a characteristic history of transient blurring of vision associated with haloes around lights due to corneal epithelial oedema (the blue end of the spectrum being nearer the source). There may also be associated ocular discomfort or frontal headache. The attacks are recurrent and are usually broken after 1–2 hours by physiological miosis (exposure to bright sunlight or sleep). During an attack the eye is usually white and in between attacks looks normal although the angle is narrow.
2. **The clinical course** without treatment is variable. Some eyes develop an acute attack and others may develop chronic angle closure.
3. **Treatment** is with prophylactic peripheral laser iridotomy.

Acute congestive angle-closure glaucoma

This is a sight-threatening emergency, involving painful loss of vision, due to sudden and total closure of the angle.

Clinical features

1. **Symptoms** in classical cases include rapidly progressive unilateral visual loss associated with periocular pain and congestion. Nausea and vomiting may occur in severe cases.

> ***NB:*** It is important to note the variability of symptoms in an attack of acute angle-closure. Some patients, particularly black people, in whom the condition is uncommon, have remarkably little pain and no congestion despite very high IOPs, the only symptom being impairment of vision. Moreover, a history of transient blurring and haloes characteristic of previous intermittent attacks is often absent.

2. **Slit-lamp biomicroscopy**
   - 'Ciliary' flush due to injection of the limbal and conjunctival blood vessels.

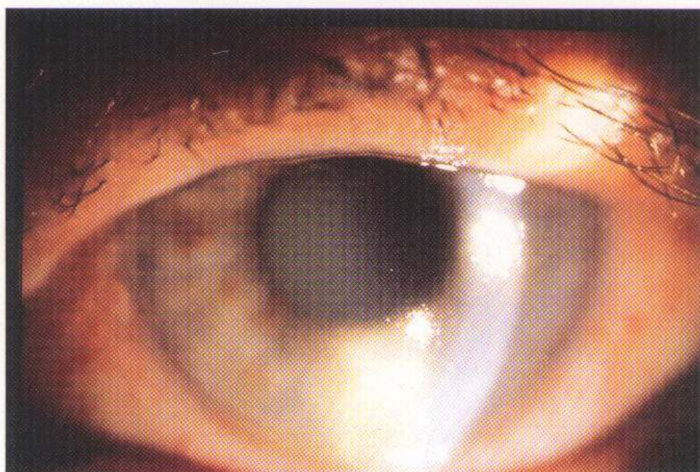


Fig. 9.61
Corneal oedema in acute angle-closure glaucoma

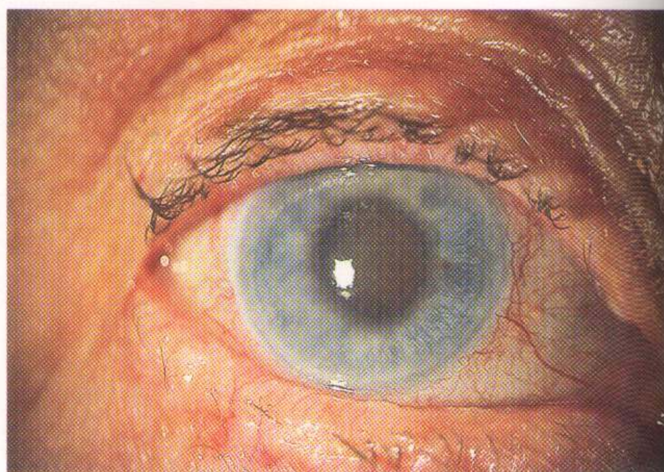


Fig. 9.63
Dilated and oval pupil in acute angle-closure glaucoma

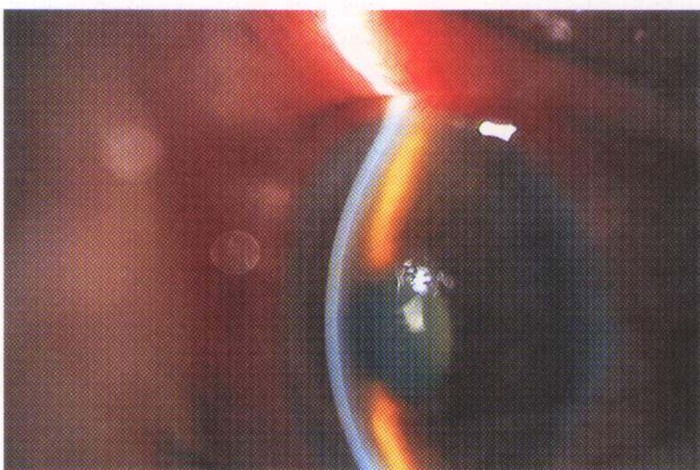


Fig. 9.62
Corneal oedema and a shallow anterior chamber in acute angle-closure glaucoma



Fig. 9.64
Gonioscopy showing complete angle closure

- Corneal oedema with epithelial vesicles and stromal thickening (Fig. 9.61).
- Shallow anterior chamber with peripheral iridocorneal contact (Fig. 9.62).
- Aqueous flare and cells may be seen once the corneal oedema has resolved.
- The pupil is vertically oval, fixed in the semi-dilated position (Fig. 9.63) and unreactive to both light and accommodation.
- The iris blood vessels are dilated.
- The IOP is severely elevated (50–100 mmHg).

3. **Gonioscopy** may need to be deferred until the corneal oedema has resolved, either with ocular hypotensive medication or with topical glycerine or hypertonic saline ointment. It is, however, vital to perform this examination in the fellow eye, which usually exhibits characteristics of latent angle closure. The affected eye shows complete peripheral iridocorneal contact (Shaffer grade 0) (Fig. 9.64).

> ***NB:*** The diagnosis should be questioned if the fellow eye does not show a narrow angle on gonioscopy.

4. **Ophthalmoscopy**, when possible, shows optic disc oedema and hyperaemia.

Differential diagnosis

1. **Secondary acute angle closure** due to an intumescent (swollen) or dislocated lens.
2. **Neovascular glaucoma** may occasionally cause a sudden onset of pain and congestion.
3. **Glaucomatocyclitic crisis** may cause severe elevation of IOP with pain and haloes.
4. **Other causes of headache** around the eye such as migraine or migrainous neuralgia (cluster headache).

Immediate treatment

1. **Acetazolamide** 500 mg intravenously and 500 mg orally (not slow-release) provided there is no vomiting.

> ***NB:*** Check for sulphonamide allergy.

2. **Topical therapy**
   - Pilocarpine 2% two drops to both eyes.

- Dexamethasone (or equivalent) q.i.d.
- A beta-blocker if there is no systemic contraindication.

3. **Analgesia** and anti-emetics as required.
4. **Patient to lie supine** for 1 hour.

> *NB:* Laser iridotomy may also be effective in relatively mild cases.

After 1 hour

Pilocarpine 2% should be repeated half to 1 hour after commencement of treatment, by which time reduction of iris ischaemia and lowering of IOP allows the sphincter pupillae to respond to the drug. There is no place for 'intensive' miotic therapy. The fellow eye is also treated prophylactically with pilocarpine 1% q.i.d. until a laser iridotomy can be performed.

After further 30 minutes

If the IOP has not fallen to below 35 mmHg, oral 50% glycerol may be administered (1 g/kg) (with caution in diabetics) and fluid intake limited for maximum effect. If the patient is unable to tolerate oral glycerol, 20% mannitol (1–2 g/kg) may be given intravenously over 45 minutes.

> *NB:* A high IOP unresponsive to ocular hypotensive medication may sometimes respond to axial corneal indentation with a squint hook or a Zeiss goniolens. If angle closure is appositional, this allows aqueous humour to force its way between the iris and cornea to the angle, thus opening it and gaining access to the trabecular meshwork. This measure may occasionally break a cycle of elevating IOP and allow it to fall.

Nd:YAG laser iridotomy

1. **The purpose** of peripheral laser iridotomy is to re-establish communication between the posterior and anterior chambers by making an opening in the peripheral iris. This will be successful only if less than 180° of the angle is closed by permanent peripheral anterior synechiae.
2. **Timing** varies with the severity of the attack and the rapidity of corneal clearing. Iridotomy has been advocated as initial treatment to break pupil block but may be difficult until the corneal thickening and iris congestion have settled (usually 48 hours). After an explanation has been given, it may be appropriate to perform a prophylactic laser iridotomy on the fellow eye in the interim period. Laser iridotomy is effective in about 75% of eyes with acute angle-closure glaucoma. Unresponsive cases may require trabeculectomy.

> *NB:* It is important to confirm that the angle is open after peripheral iridotomy even if the IOP is normal.

Postcongestive angle-closure glaucoma

Clinical settings

Postcongestive angle-closure glaucoma refers to the aftermath of an attack of acute angle closure. It may be seen in the following three clinical settings:

1. **Postsurgical**. Here the IOP is normalized by successful peripheral iridotomy. Occasionally, even after peripheral iridotomy, with the angle open 180° or more, IOP may still be elevated due to associated trabecular damage. Medical therapy or trabeculectomy may be needed to control the IOP.
2. **Spontaneous angle reopening** without treatment may occur in a few cases; management is as for intermittent angle closure.
3. **Ciliary body shutdown**. This involves temporary cessation of aqueous secretion due to ischaemic damage to the ciliary epithelium. Subsequent recovery of ciliary function may lead to chronic elevation of IOP with cupping and field loss.

Clinical features

1. **Slit-lamp biomicroscopy**
   - Folds in Descemet membrane (Fig. 9.65), if the IOP has been reduced rapidly.
   - Fine pigment granules on the corneal endothelium.
   - Aqueous flare and cells.
   - Stromal iris atrophy with a spiral-like configuration; fine pigment granules on the surface of the iris (Fig. 9.66).
   - A fixed and semi-dilated pupil due to a combination of paralysis of the sphincter and posterior synechiae (Fig. 9.67).
   - Glaukomflecken characterized by small, grey-white, anterior subcapsular or capsular lens opacities in the pupillary zone are diagnostic of a previous congestive attack (Fig. 9.68). These represent focal necrosis of the lens epithelium.
   - The IOP may be normal, subnormal or elevated.

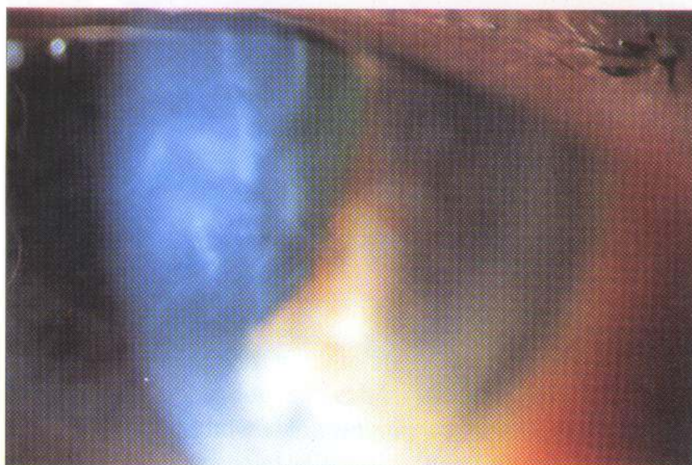


Fig. 9.65
Folds in Descemet membrane and residual corneal oedema in postcongestive angle-closure glaucoma

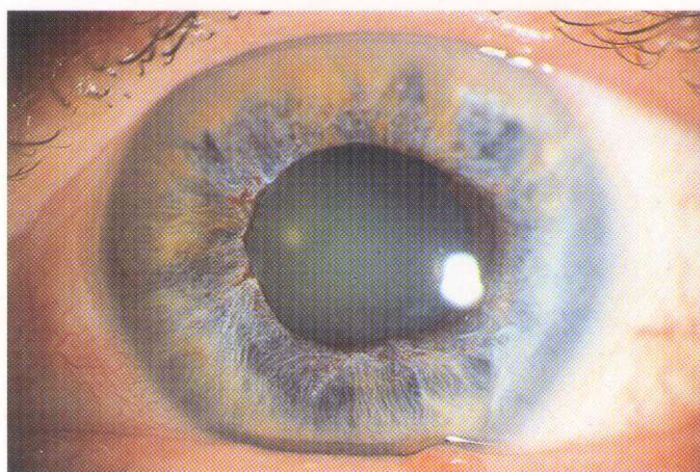


Fig. 9.66
Stromal iris atrophy in postcongestive angle-closure glaucoma

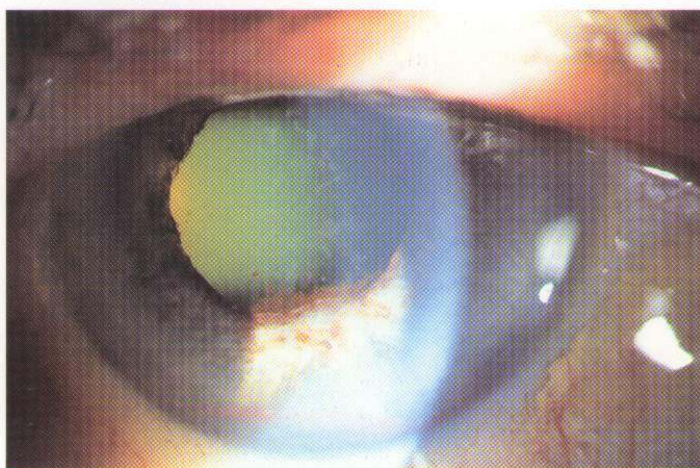


Fig. 9.67
Posterior synechiae in postcongestive angle-closure glaucoma

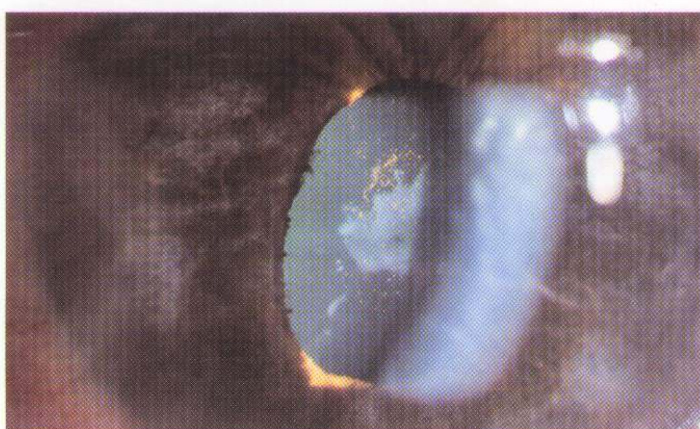


Fig. 9.68
Anterior subcapsular lens opacities (glaukomflecken) in postcongestive angle-closure glaucoma

2. **Gonioscopy** shows a narrow angle which may be open or partly closed. If open, trabecular hyperpigmentation may be present. A straight line of pigment may be seen anterior to Schwalbe line at the site of previous iridocorneal contact.

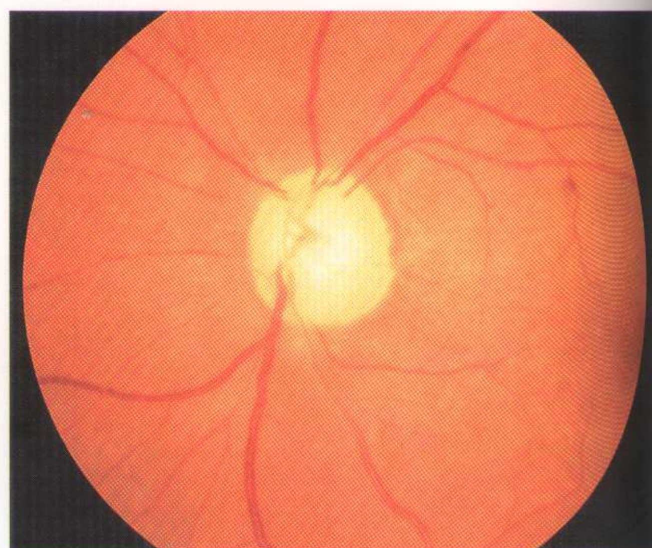


Fig. 9.69
Optic atrophy following acute angle-closure glaucoma (Courtesy of J. Salmon)

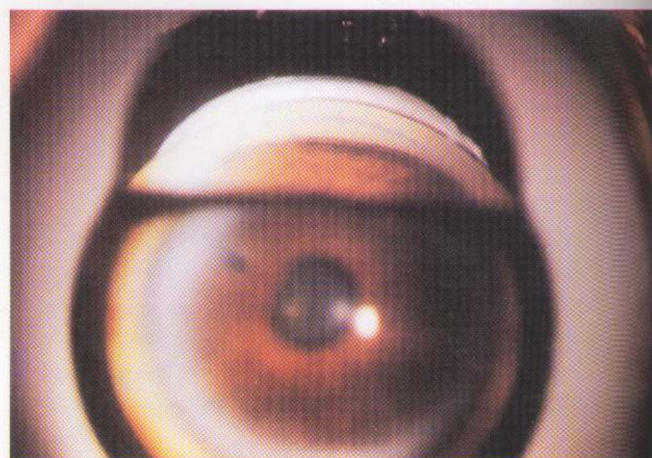


Fig. 9.70
'Creeping' angle closure (Courtesy of J. Salmon)

3. **Ophthalmoscopy** may reveal congestion of the optic disc and choroidal folds if the IOP is very low. The disc may be atrophic as a result of infarction (Fig. 9.69).

Chronic angle-closure glaucoma

Pathogenesis

1. **Type 1** (creeping) is caused by gradual and progressive synechial angle closure which always starts superiorly and spreads circumferentially (Fig. 9.70). This may be caused by anteriorly situated ciliary processes; many eyes have a plateau iris configuration (*see* below).
2. **Type 2** is caused by synechial angle closure as a result of intermittent (subacute) attacks secondary to pupillary block.
3. **Type 3** (mixed) is caused by a combination of POAG with narrow angles usually associated with the long-term use of miotics. It is commonly diagnosed on gonioscopy at the time of laser trabeculoplasty.

Clinical features

These are similar to POAG. Gonioscopy shows a variable degree of angle closure, although permanent peripheral anterior synechiae do not usually develop until late. The diagnosis will be missed unless gonioscopy is performed on all glaucomatous eyes.

Treatment

1. **Type I** (creeping) is initially treated by laser iridotomy to eradicate any element of pupil block. Any residual elevation of IOP is then treated medically. If this fails, trabeculectomy will be required.
2. **Type 2** will already have undergone iridotomy. Medical therapy should be added as necessary.
3. **Type 3** (mixed) will already be on medical therapy for POAG and should be treated by laser iridotomy.

Plateau iris

1. **Plateau iris configuration** is characterized by a closed anterior chamber angle in association with a flat iris plane and a deep central anterior chamber. An anterior position of the ciliary processes results in an abnormal configuration of the peripheral iris. Although this mechanism of angle closure is rare in white people, it is not uncommon in South-East Asians.
2. **Plateau iris syndrome** describes acute angle closure which occurs with pupillary dilatation despite a patent iridotomy. The syndrome tends to occur at a younger age than angle closure with pupillary block. When the pupil dilates, the peripheral iris becomes 'bunched up' and occludes the trabeculum (Fig. 9.71). All the features of acute congestive angle closure are present except that the axial anterior chamber depth is normal and the iris plane is flat rather than convex.
3. **Treatment** is with pilocarpine 1% drops after the performance of a laser peripheral iridotomy. It may also be possible to flatten the 'hump' in the peripheral iris with argon laser (gonioplasty).

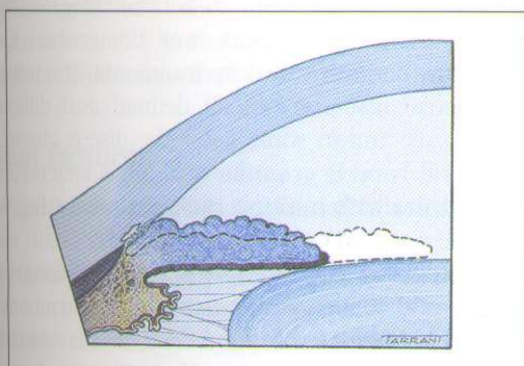


Fig. 9.71
Angle closure in the plateau iris syndrome

Pseudoexfoliative glaucoma

Pseudoexfoliation syndrome

Introduction

The pseudoexfoliation (PEX) syndrome is a relatively common but easily overlooked cause of chronic open-angle glaucoma. When an eye with PEX develops a secondary trabecular block glaucoma the condition is referred to as PEX glaucoma or glaucoma capsulare. Although PEX is more common in females, males appear to be at higher risk of developing glaucoma. Although no clear hereditary pattern has been established, the condition is a particularly common cause of glaucoma in Scandinavia and is also associated with a gene locus at 2p16. PEX should be differentiated from very rare true exfoliation, which involves lamellar splitting of the lens capsule secondary to infra-red damage.

Pathogenesis

In PEX a grey-white, fibrillogranular, extracellular, matrix material similar to amyloid, is deposited on the anterior lens capsule, zonules, ciliary body, iris, trabeculum, anterior vitreous face and conjunctiva. Secondary trabecular block glaucoma is thought to result from a combination of 'clogging up' of the trabeculum by pseudoexfoliative material and/or pigment released from the iris, as well as trabecular endothelial dysfunction. The material is produced by abnormal basement membranes of ageing epithelial cells in the trabeculum, equatorial lens capsule, iris and ciliary body.

> ***NB:*** In addition to its occurrence within the eye, exfoliative fibrillopathy has been reported in skin and visceral organs, suggesting that the PEX syndrome may be an ocular manifestation of a systemic disorder.

Clinical features

1. **Cornea**
   a. *PEX* on the endothelium may mimic inflammatory keratic precipitates.
   b. ***Pigment deposition*** on the endothelium is usually diffuse although occasionally it may take the form of a Krukenberg spindle (*see* below).
   c. ***Endothelial cells*** are reduced in number and morphologically abnormal with a propensity to decompensation, even with a moderate rise in IOP.
2. **Anterior chamber** may exhibit mild aqueous flare due to breakdown of the iris blood–aqueous barrier (pseudouveitis).
3. **Iris**
   a. *PEX* on the pupillary margin (Fig. 9.72).
   b. ***Sphincter atrophy*** characterized by 'moth-eaten' transillumination defects (Fig. 9.73), most evident in

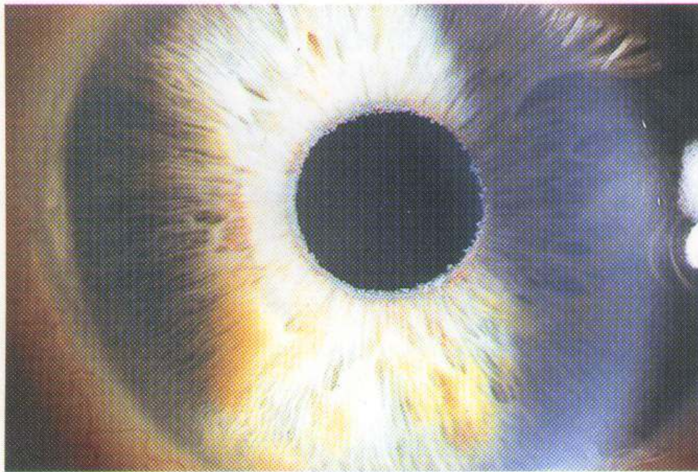
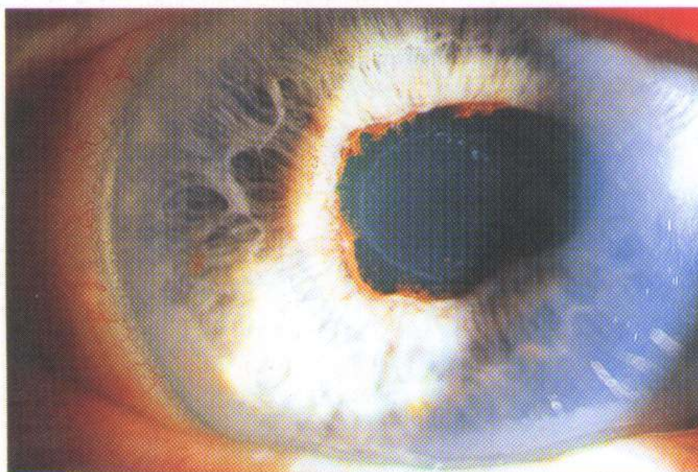

Fig. 9.72
Pseudoexfoliative material on the pupillary border


Fig. 9.73
Sphincter atrophy seen on transillumination in the pseudoexfoliation syndrome


Fig. 9.74
Posterior synechiae in the pseudoexfoliation syndrome

eyes with pupillary ruff defects. It is associated with poor pupillary dilatation.

c. ***Pigment dispersion*** may be precipitated by mydriasis or surgery. On the iris sphincter the pigment granules have a whorl-like configuration whereas in the periphery they are scattered more diffusely.

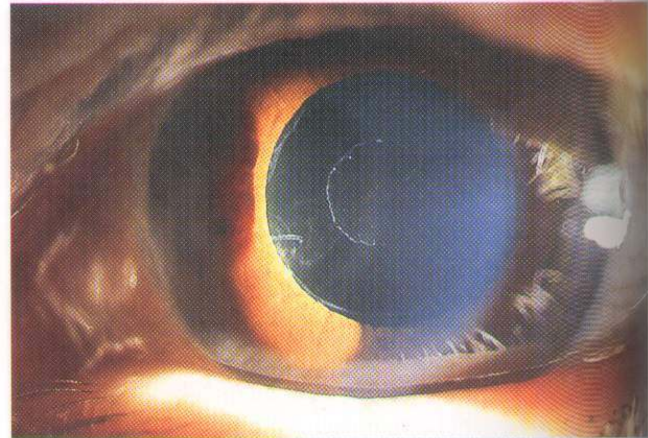

Fig. 9.75
Central disc and a peripheral band of pseudoexfoliative material


Fig. 9.76
Peripheral band of pseudoexfoliative material

d. ***Intrastromal haemorrhages*** may develop on pharmacological mydriasis.

e. ***Posterior synechiae*** may contribute to poor pupillary dilatation (Fig. 9.74).

4. Lens

a. ***PEX*** on the anterior lens surface. The constant rubbing of the pupil scrapes the material off the mid-zone of the lens, giving rise to a central disc and a peripheral band of PEX, with a clear zone in between (Fig. 9.75). The central disc is translucent, well demarcated and its edges may contain rolled-up fragments. The margin of the central disc may be ill defined and difficult to distinguish, and in some cases the disc is absent. The peripheral band is granular and has a well-delineated inner border with multiple radial striations (Fig. 9.76). It can be detected only under mydriasis.

b. ***Zonular instability*** is caused by alterations in the zonules and their insertions into the ciliary body and lens. This may give rise to phacodonesis, lens subluxation/dislocation and an increased incidence of zonular dialysis and vitreous loss during cataract surgery.

c. ***Nuclear cataract*** occurs commonly.



Fig. 9.77
Trabecular hyperpigmentation with a Sampaolesi line in the pseudoexfoliation syndrome

5. **Gonioscopy**
   a. *Trabecular hyperpigmentation* is common and is usually most marked inferiorly. The pigment lies on the surface of the trabeculum and has a patchy distribution (Fig. 9.77). A scalloped band of pigment running on to or anterior to Schwalbe line (Sampaolesi line) is also frequently seen.
   b. *PEX* may be deposited in the trabeculum and give rise to a 'dandruff-like' appearance.
   c. *Narrow angles* are present in some cases; even in eyes with wide open angles, the IOP may become elevated when the pupil is dilated.

Pseudoexfoliative glaucoma

Risk factors

- The cumulative risk of glaucoma in eyes with pseudoexfoliation is 5% at 5 years and 15% at 10 years. Individuals with PEX should be informed of this risk and advised to undergo annual ocular examination.
- A patient with unilateral pseudoexfoliative glaucoma and PEX in the fellow eye is at high risk (50% in 5 years) of developing glaucoma in the fellow eye.
- A patient with unilateral pseudoexfoliation glaucoma who does not have PEX in the fellow eye is at very small risk of developing glaucoma in the normal eye.

Clinical features

1. **Presentation** is usually in the seventh decade, which is later than POAG.
2. **Signs.** The majority of patients have a chronic open-angle glaucoma which is usually unilateral. Occasionally the IOP may rise acutely despite the angle being wide open; this may be confused with primary angle-closure glaucoma. The degree of angle hyperpigmentation correlates with the severity of glaucoma.

Treatment

1. **Medical** treatment is the same as for POAG. However, despite initial success in most cases, there is a high incidence of late failure and patients are likely to require laser therapy or surgery.
2. **Laser trabeculoplasty** is particularly effective, possibly because of trabecular hyperpigmentation. However, after an initial good response a gradual late rise of IOP occurs so that after 4 years the results are the same as in POAG.
3. **Early trabeculectomy** may be advantageous. It has the same success rate as in POAG, with no unusual complications.

Prognosis

This is poorer than with POAG, since the IOP is often significantly elevated and may also exhibit great fluctuation so that severe damage may develop rapidly. It is therefore important to monitor patients closely until the IOP is brought under control.

Pigmentary glaucoma

Pigment dispersion syndrome

The pigment dispersion syndrome (PDS) is a usually bilateral condition characterized by the liberation of pigment granules from the iris pigment epithelium and their deposition throughout the anterior segment. PDS primarily affects white people, and may be inherited as an autosomal dominant trait with variable penetrance. Two gene loci have been identified on chromosomes 7 and 8. Myopia predisposes to the phenotypical manifestations and the development of a secondary open-angle 'pigmentary' glaucoma.

Pathogenesis

Pigment shedding is caused by the mechanical rubbing of the posterior pigment layer of the iris against packets of lens zonules as a result of excessive posterior bowing of the mid-peripheral portion of the iris. The pigment epithelium itself may be abnormally susceptible to shedding; in some patients strenuous exercise may precipitate episodes of pigment dispersion associated with a rise in IOP. The pigment granules are released into the aqueous humour, dispersed by aqueous currents and deposited on all anterior chamber structures, including the zonular fibres and ciliary body. Elevation of IOP appears to be caused by pigmentary obstruction of the intertrabecular spaces and damage to the trabeculum secondary to denudation, collapse and sclerosis. It is postulated that an increase in anterior chamber pressure (relative to the posterior chamber) occurs due to 'reverse' pupil block, with resultant posterior bowing of the iris and irido-zonular touch. This is supported by

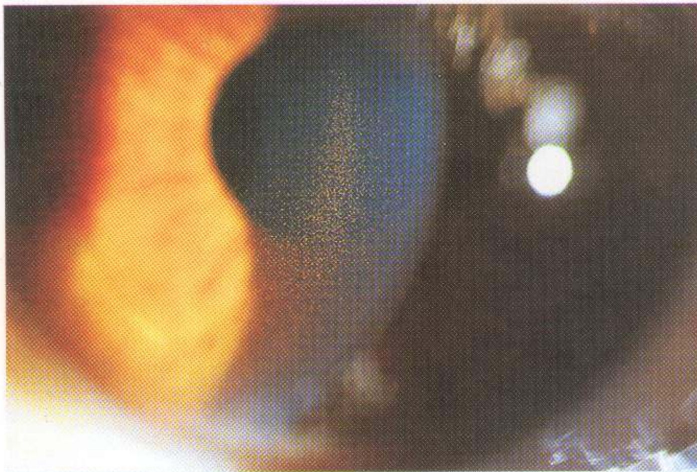


Fig. 9.78
Krukenberg spindle in the pigment dispersion syndrome

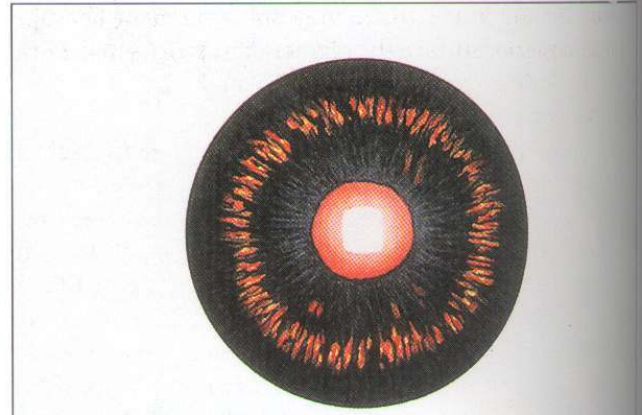


Fig. 9.81
Mid-peripheral iris transillumination defects in the pigment dispersion syndrome



Fig. 9.79
Very deep anterior chamber in the pigment dispersion syndrome



Fig. 9.82
Trabecular hyperpigmentation in the pigment dispersion syndrome

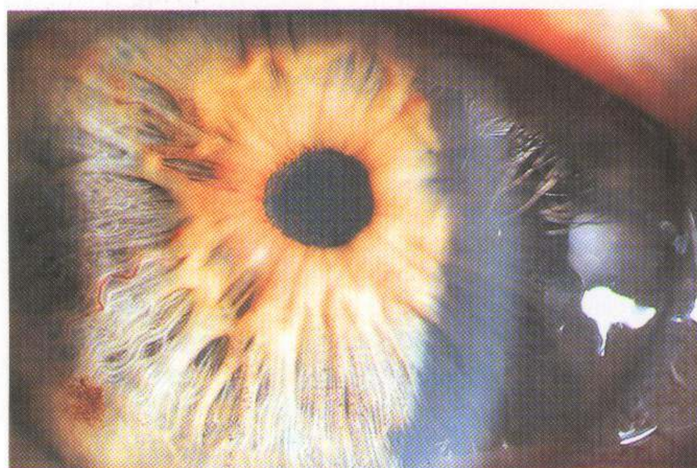


Fig. 9.80
Pigment granules on the iris in the pigment dispersion syndrome

the observation that neutralization of reverse pupil block with peripheral iridotomy flattens the iris and decreases irido-zonular contact.

Clinical features

1. **The cornea** manifests pigment deposition on the endothelium in a vertical spindle-shaped distribution (Krukenberg spindle) (Fig. 9.78). The size and density of the deposit are usually proportional to the extent of associated iris atrophy. The Krukenberg spindle, although common, is neither universal nor pathognomonic of PDS, and in long-standing cases may be more difficult to detect because it tends to become smaller and lighter in colour.
2. **The anterior chamber** is very deep (Fig. 9.79); melanin granules may be seen floating in the aqueous.
3. **Iris**
   a. ***Fine pigment granules*** are preferentially deposited within its furrows (Fig. 9.80). This may render the iris progressively darker, giving rise to heterochromia iridis in asymmetrical involvement.
   b. ***Iris pigment epithelial atrophy*** due to shedding of pigment from the mid-periphery gives rise to characteristic radial slit-like transillumination defects (Fig. 9.81). If asymmetrical, the eye with more iris atrophy may exhibit a slightly larger pupil.

4. **Lens.** The anterior surface may show pigment deposits. On the posterior surface the pigment tends to form a line at the site of vitreolenticular adhesion.
5. **Gonioscopy**
   a. *Wide open angle* with characteristic mid-peripheral iris concavity that may increase with accommodation.
   b. *Trabecular hyperpigmentation* is most marked over the posterior trabeculum (Fig. 9.82). In contrast with the coarse pigmentation seen in PEX, that in PDS is finer and appears to lie both on and within the trabecular meshwork. It also has a more homogeneous appearance and forms a dense band involving the entire circumference of the angle uniformly. Pigment may also be seen on or anterior to Schwalbe line.
6. **The fundus** may show areas of lattice degeneration which may be responsible for an increased risk of retinal detachment. Pigment deposition may also be seen in the perioral retina.

Pigmentary glaucoma

Risk factors

Up to one-third of patients with PDS eventually develop ocular hypertension or chronic open-angle glaucoma. Men are affected twice as frequently as women. It is therefore important to regularly follow patients with the condition, particularly myopic males with Krukenberg spindles. However, initial IOP, cup–disc ratio and degree of trabecular hyperpigmentation are not helpful in identifying those who will eventually develop glaucoma. Patients with pigmentary glaucoma have an increased incidence of steroid responsiveness. Although PDS is rare in black patients, they are at increased risk of developing glaucoma which is of a more severe form than that found in white patients.

Clinical features

1. **Presentation** is usually with chronic glaucoma most commonly in the third and fourth decades, although in women it tends to develop 10 years later. Occasionally the sudden release of pigment granules following vigorous movement of the pupil or strenuous physical exercise may precipitate an acute rise in IOP, with corneal oedema and haloes.
2. **The IOP** may initially be very unstable, so that a single normal reading does not exclude glaucoma. Some patients exhibit higher levels and wider fluctuations of IOP than in POAG, and at the time of diagnosis it is common to find advanced disease in one eye and relatively mild damage in the other.

Treatment

1. **Medical** treatment is similar to that of POAG. Miotics may, theoretically, be of particular benefit because they decrease irido-zonular contact in addition to facilitating aqueous outflow. However, they carry the disadvantage of exacerbating myopia.
2. **Laser trabeculoplasty** is often initially effective, although younger patients appear to respond better. It is important not to over-treat eyes with heavily pigmented angles and to start at a relatively low-power laser setting. At least one-third of patients will require trabeculectomy within 5 years of laser trabeculoplasty.
3. **Laser iridotomy** may be effective in preventing further pigment deposition by reversing iris concavity.
4. **Trabeculectomy** is required in patients unresponsive to medical therapy and laser trabeculoplasty, although the results are less predictable in younger patients. Operative use of adjunctive antimetabolites may improve surgical outcome. A higher percentage of patients with pigmentary glaucoma require surgery as compared with POAG and men require it earlier.

Prognosis

This is relatively good and over time the control of IOP becomes easier. Occasionally the IOP may spontaneously revert to normal. This may or may not be associated with a decrease in trabecular pigmentation. Patients with such undetected previous pigmentary glaucoma may later be erroneously diagnosed as having normal-tension glaucoma.

Differential diagnosis

1. **POAG** may be associated with a hyperpigmented trabeculum. However, the pigment tends to be concentrated in the inferior sector of the angle, unlike in the PDS. Patients with POAG are also usually older and lack Krukenberg spindles and iris transillumination defects.
2. **Pseudoexfoliative glaucoma** may exhibit trabecular hyperpigmentation and pigment dispersion. However, transillumination defects are evident at the margin of the pupil rather than in the periphery. In contrast to pigmentary glaucoma, pseudoexfoliative glaucoma usually affects patients over the age of 60 years, is unilateral in 50% of cases and has no predilection for a myopic refractive error.
3. **Pseudophakic pigmentary glaucoma** occurs in the context of rubbing of the haptics and optics of a posterior chamber intraocular lens against the posterior surface of the iris, with resultant pigment dispersion and outflow obstruction.
4. **Anterior uveitis** may result in trabecular hyperpigmentation and iris atrophy. Clustered small old pigmented keratic precipitates may be mistaken for a Krukenberg spindle on cursory examination.
5. **Subacute angle-closure glaucoma** may be associated with a heavily pigmented trabeculum where the iris root has been in contact with the angle.

Neovascular glaucoma

Introduction

Pathogenesis

Neovascular glaucoma (NVG) is a relatively common and serious condition which occurs as a result of iris neovascularization (rubeosis iridis). The common aetiopatho-

genic factor is severe, diffuse and chronic retinal ischaemia. It is postulated that hypoxic retina produces vasoproliferative growth factors in an attempt to revascularize hypoxic areas. Apart from inducing retinal neovascularization (proliferative retinopathy) such factors also diffuse into the anterior segment and initiate rubeosis iridis and neovascularization in the angle of the anterior chamber. The latter initially impairs aqueous outflow in the presence of an open angle and later contracts to produce a secondary angle-closure glaucoma which is usually severe and relentless. NVG can often be prevented by timely treatment of ischaemic retina by laser photocoagulation.

Causes

1. **Ischaemic central retinal vein occlusion** accounts for 36% of cases. Approximately 50% of eyes develop NVG following ischaemic central retinal vein occlusion. Extensive peripheral retinal capillary non-perfusion on fluorescein angiography is the most valuable predictor of the risk of subsequent NVG, although in some patients non-ischaemic occlusion may subsequently become ischaemic. Glaucoma typically occurs 3 months after the occlusion ('100-day glaucoma') but intervals from 4 weeks to 2 years have been documented.
2. **Diabetes mellitus** accounts for 32% of cases. Patients with long-standing diabetes (10 years or more) with proliferative retinopathy are at particular risk. The risk of glaucoma is decreased by appropriate panretinal photocoagulation and increased by cataract extraction, particularly if the posterior capsule is breached. Frequent review is essential during the first 4 postoperative weeks, which represent the crucial period for the development of rubeosis iridis. Pars plana vitrectomy may also precipitate rubeosis iridis if inadequate laser therapy is applied or tractional retinal detachment remains.
3. **Miscellaneous** causes include carotid obstructive disease, central retinal artery occlusion, intraocular tumours, long-standing retinal detachment and chronic intraocular inflammation.

Classification

Despite a degree of overlap it is convenient to divide NVG into the following three stages:

- Rubeosis iridis.
- Secondary open-angle glaucoma.
- Secondary synechial angle-closure glaucoma.

Rubeosis iridis

Clinical features

- Tiny dilated capillary tufts or red spots develop at the pupillary margin (Fig. 9.83) and may be missed unless the iris is examined carefully under high magnification.
- The new vessels grow radially over the surface of the iris (Fig. 9.84) towards the angle, sometimes joining dilated blood vessels at the collarette. At this stage the IOP may still be normal; and the new vessels may regress either spontaneously or with treatment.

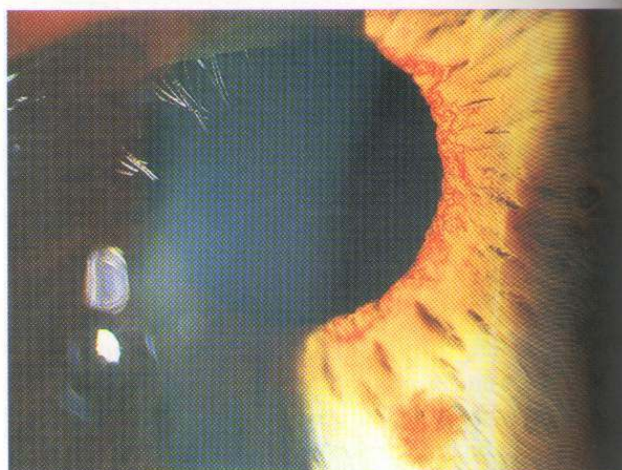


Fig. 9.83
Rubeosis iridis on the pupillary border

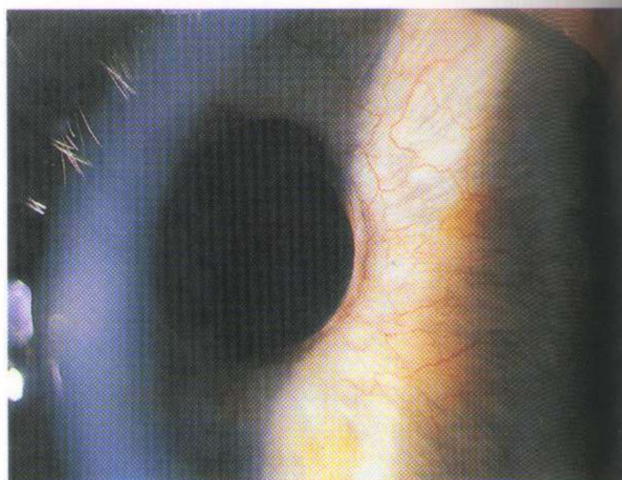


Fig. 9.84
Moderate rubeosis iridis

> ***NB:*** Angle neovascularization in the absence of pupillary involvement may occur after central retinal vein occlusion. It is therefore important to perform careful gonioscopy in eyes at high risk even when the pupillary border is uninvolved.

Management

1. **Panretinal photocoagulation**, if performed early, is often effective in inducing regression of the new vessels and preventing subsequent progression to glaucoma.
2. **Retinal surgery.** If rubeosis develops or persists following vitrectomy in a diabetic patient with residual retinal detachment, retinal reattachment should be attempted, since if successful, the rubeosis will frequently regress. Additional panretinal photocoagulation will also be beneficial.

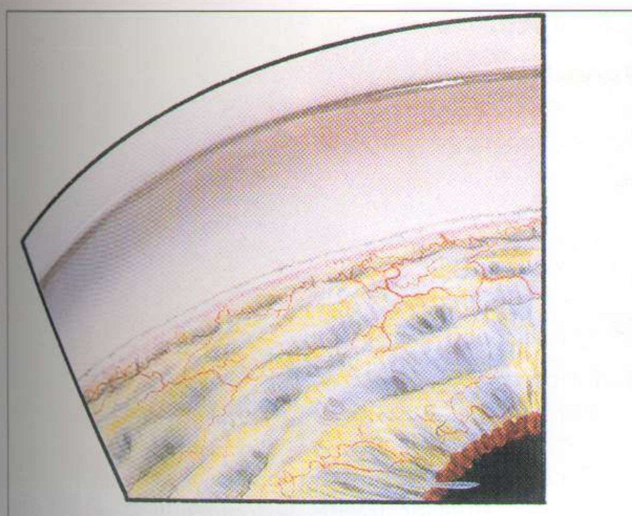


Fig. 9.85
Early angle neovascularization

Secondary open-angle glaucoma

Clinical features

The new blood vessels continue to grow across the iris surface towards the iris root. The neovascular tissue then proliferates across the face of the ciliary body and scleral spur to invade the angle (Fig. 9.85). Here the new blood vessels arborize and form a fibrovascular membrane, which blocks the trabeculum and gives rise to a secondary open-angle glaucoma.

Treatment

1. **Medical** treatment is as for POAG but miotics should be avoided. Topical atropine 1% and intensive topical steroids should be given to reduce inflammation and promote comfort.
2. **Panretinal photocoagulation** should still be performed even if the IOP is adequately controlled medically although this will not influence the fibrous component of the fibrovascular membrane.

Secondary angle-closure glaucoma

This is caused by contraction of fibrovascular tissue in the angle with pulling of the peripheral iris over the trabeculum. The angle thus closes circumferentially in a zipper-like fashion.

Clinical features

- Visual acuity is severely reduced.
- Congestion of the globe and pain.
- Very high IOP and corneal oedema.
- Aqueous flare due to leakage of proteins from the iris new vessels.
- Severe rubeosis iridis (Fig. 9.86) with distortion of the pupil and ectropion uveae due to radial contraction of fibrovascular tissue (Fig. 9.87).

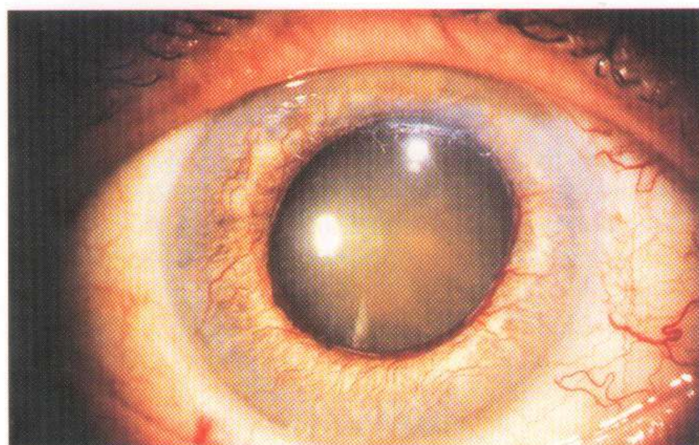


Fig. 9.86
Severe rubeosis iridis (Courtesy of J. Salmon)

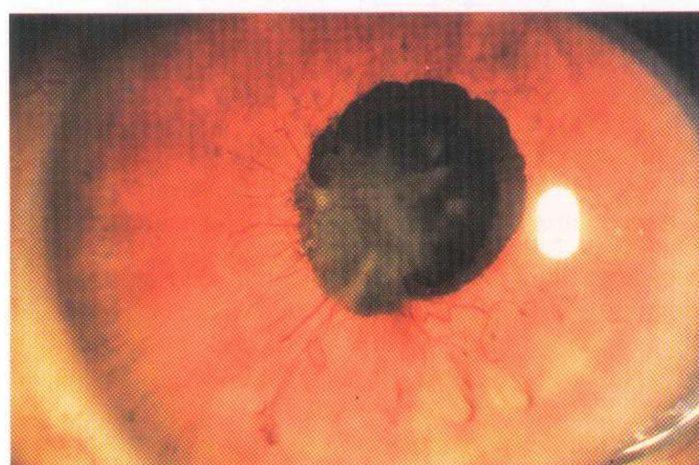


Fig. 9.87
Distortion of the pupil and ectropion uveae in severe rubeosis iridis (Courtesy of J. Salmon)

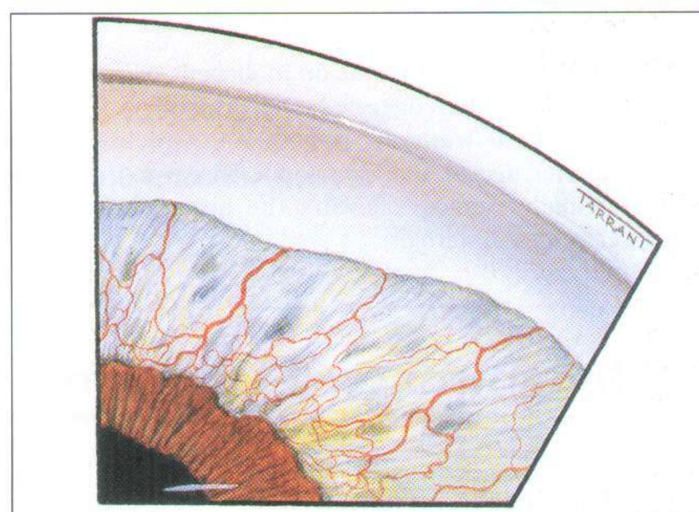


Fig. 9.88
Total synechial angle closure

- Gonioscopy shows synechial angle closure with inability to visualize any angle structures posterior to Schwalbe line (Fig. 9.88).

Treatment

This is aimed mainly at relieving pain, as the prognosis for maintaining visual function is extremely poor.

1. **Medical** treatment is with topical and systemic hypotensive agents except miotics. Topical atropine and steroids may decrease the inflammation and make the eye more comfortable and less congested, even if the IOP remains high.
2. **Retinal ablation** is performed by argon laser, if possible. In eyes with opaque media this can be achieved by trans-scleral diode laser photocoagulation or cryotherapy.
3. **Surgery** may be considered if vision is 'hand movements' or better. The two options are trabeculectomy with adjunctive mitomycin C or artificial filtering shunts.

> *NB:* Although surgery may succeed in lowering IOP, many eyes subsequently lose light perception or become phthisical, so that the main benefit is that of pain relief.

4. **Cyclodestruction** by trans-scleral diode laser may effectively control IOP and render the eye more comfortable, particularly in conjunction with medical therapy.
5. **Retrobulbar alcohol injection** is useful in relieving pain but it may cause permanent ptosis and does not relieve congestion.
6. **Enucleation** if all else fails.

Differential diagnosis

1. **Primary congestive angle-closure glaucoma.** NVG may occasionally present with sudden onset of pain, congestion and corneal oedema. Gonioscopy after clearing the cornea with ocular hypotensive agents and/or topical glycerine is useful to differentiate the two. Moreover, the fellow eye manifests a normal angle.
2. **Postvitrectomy inflammation** in diabetic patients may be associated with congested and prominent iris vasculature and a transient rise in IOP, which may be mistaken for neovascular glaucoma. However, these features usually resolve following the intensive administration of topical steroids.

Inflammatory glaucoma

Introduction

Glaucoma secondary to intraocular inflammation frequently presents a diagnostic and therapeutic challenge. The elevation of IOP may be transient and innocuous, or persistent and severely damaging. Secondary glaucoma is the most common cause of blindness in children and young adults with chronic anterior uveitis.

Classification

1. Angle closure with pupil block.
2. Angle closure without pupil block.
3. Open angle.
4. Specific hypertensive uveitis syndromes.
   - Fuchs uveitis syndrome.
   - Posner–Schlossman syndrome.

Diagnostic problems

1. **Fluctuation of IOP** may be dramatic in uveitic glaucoma and phasing may be helpful in patients with borderline IOP.
2. **Ciliary body shutdown** caused by acute exacerbation of chronic anterior uveitis is frequently associated with lowering of IOP that may mask the underlying tendency to glaucoma. Even eyes with considerably elevated IOP (30–35 mmHg) may become hypotonous during acute exacerbations of uveitis. Return of ciliary body function with subsidence of uveitis may be associated with a rise in IOP in the presence of permanently compromised outflow facility.

> *NB:* It is important to perform gonioscopy in eyes with anterior uveitis and to continue monitoring the IOP as the inflammation resolves.

3. **The mechanisms** of elevation of IOP may be uncertain; multiple mechanisms may be involved. Steroid-responders often represent a therapeutic challenge.

Angle-closure glaucoma with pupil block

Pathogenesis

Secondary pupil block glaucoma is caused by posterior synechiae extending for 360° (seclusio pupillae) which obstruct aqueous flow from the posterior to the anterior chamber. The resultant increased pressure in the posterior chamber produces anterior bowing of the peripheral iris (iris bombé), with shallowing of the anterior chamber and apposition of the peripheral iris to the trabeculum and peripheral cornea. Such an inflamed iris easily sticks to the trabeculum; and the iridocorneal contact becomes permanent with the development of peripheral anterior synechiae (PAS).

> *NB:* Angle-closure glaucoma with pupil block is uncommon; most eyes with seclusio pupillae exhibit a normal or subnormal IOP due to concomitant chronic ciliary body shutdown.

Clinical features

1. **Slit-lamp biomicroscopy** shows seclusio pupillae, iris bombé and a shallow anterior chamber (Fig. 9.89).

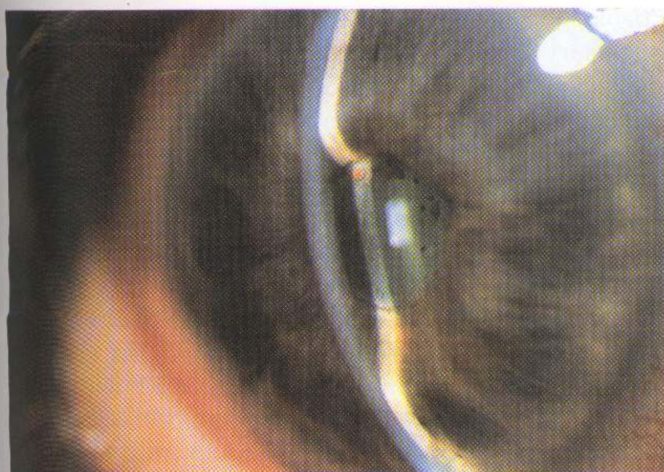


Fig. 9.89
Iris bombé and a very shallow anterior chamber

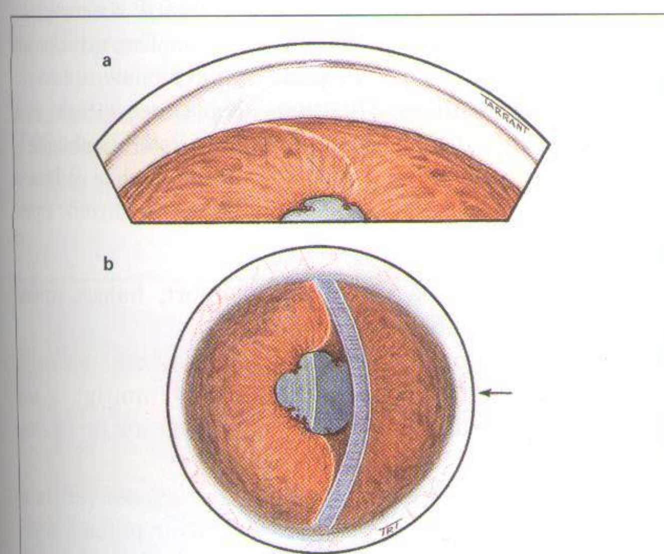


Fig. 9.90
Secondary pupil block angle closure. (a) Gonioscopic view; (b) slit-lamp view

2. **Gonioscopy** shows angle closure from iridotrabecular contact (Fig. 9.90). Indentation gonioscopy with a Zeiss four-mirror goniolens, or equivalent, may be used to assess the extent of appositional as opposed to synechial angle closure.

Treatment

1. **Medical** treatment is initially with topical aqueous suppressants although short-term systemic carbonic anhydrase inhibitors may be required in severe cases.

> NB: The following drugs should be avoided in uveitic glaucoma:
> - Prostaglandin analogues enhance breakdown of the blood–aqueous barrier and may exacerbate cystoid macular oedema. They have rarely been reported to cause acute anterior uveitis.
> - Pilocarpine is also contraindicated because it will promote the development of posterior synechiae.

2. **Laser iridotomy** is performed to re-establish communication between the posterior and anterior chambers. This will eliminate only the element of pupil block and will therefore be effective in lowering IOP only if at least 25% of the angle is still open. Intensive topical steroid therapy may help to minimize post-laser inflammation. It is recommended that several large openings be made and the patient examined at frequent intervals to ensure that they remain patent. Surgical iridectomy may be considered if the laser iridotomy closes.
3. **Trabeculectomy** with adjunctive antimetabolites may be required in eyes with permanent angle closure. Trabeculectomy alone has a high failure rate because patients tend to be young and the conjunctiva has frequently been subjected to chronic exposure to preservatives from steroid and mydriatic drops.
4. **Artificial filtering shunts** may be required in resistant cases.
5. **Cycloablation** when other modalities fail.

Angle-closure glaucoma without pupil block

1. **Pathogenesis**. Chronic anterior uveitis causes the deposition of inflammatory debris in the angle, subsequent organization and contraction of which pulls the peripheral iris over the trabeculum, thereby causing gradual and progressive synechial angle closure (Fig. 9.91) with eventual elevation of IOP. The eye with a pre-existing narrow angle may be at higher risk, as may one with granulomatous inflammation with inflammatory nodules in the angle.
2. **Clinical features**. The anterior chamber is deep but gonioscopy shows extensive angle closure by PAS (Fig. 9.92).
3. **Treatment** is similar to secondary angle-closure glaucoma except that iridectomy is not indicated.

Open-angle glaucoma

In acute anterior uveitis

Here the IOP is usually normal or subnormal due to concomitant ciliary shutdown. Occasionally, however, a

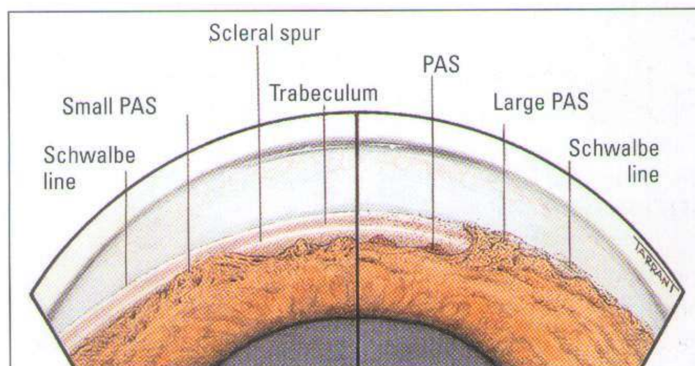


Fig. 9.91
Partial angle closure by peripheral anterior synechiae



Fig. 9.92
Extensive peripheral anterior synechiae

secondary open-angle glaucoma develops due to obstruction of aqueous outflow, most commonly as the acute inflammation is subsiding and ciliary body function is returning. This effect, which is often transient and innocuous, may be steroid-induced or caused by a combination of the following mechanisms:

1. **Trabecular obstruction** by inflammatory cells and debris which may be associated with increased aqueous viscosity due to leakage of proteins from the inflamed iris blood vessels.
2. **Acute trabeculitis** involving inflammation and oedema of the trabecular meshwork with secondary diminution of intertrabecular porosity may result in a reduction in outflow facility. It is thought that this is relevant in anterior uveitis associated with herpes zoster and herpes simplex.
3. **Prostaglandins** may be associated with raised IOP although the exact mechanism is uncertain.

In chronic anterior uveitis

Here the main mechanism for reduced outflow facility is thought to be trabecular scarring and/or sclerosis secondary to chronic trabeculitis. The exact incidence and importance of this mechanism are, however, difficult to determine as most eyes also have some degree of synechial angle closure. Because of the variable appearance of the angle on gonioscopy, definitive diagnosis of trabecular damage is difficult. Theoretically, the angle should be open and, in some eyes, a gelatinous exudate resembling 'mashed potatoes' is seen on the trabeculum. Treatment is as for secondary synechial angle-closure glaucoma.

Glaucoma in Fuchs uveitis syndrome

Fuchs uveitis syndrome (FUS) is an idiopathic, unilateral, chronic, non-granulomatous, anterior uveitis with an insidious onset, which is resistant to steroid therapy (*see* Chapter 10). The most common complication is cataract. Secondary open-angle glaucoma, probably due to trabecular sclerosis, occurs in about 30% of cases; patients should therefore be screened at 6-monthly intervals. Elevated IOP initially intermittent, later becomes constant. Occasionally the pressure rise may be precipitated by surgery. Treatment is similar to that of other types of uveitic glaucoma.

Posner–Schlossman syndrome

Posner–Schlossman syndrome (glaucomatocyclitic crisis) is characterized by recurrent attacks of unilateral, acute secondary open-angle glaucoma associated with mild anterior uveitis. The cause of the raised IOP is presumed to be acute trabeculitis. This very rare condition typically affects young adults, 40% of whom are positive for HLA-Bw54. Males are affected more frequently than females. The IOP is elevated for between a few hours and several days. The attacks are unilateral, although 50% of patients have bilateral involvement at different times. The intervals between attacks vary and, with time, usually become longer. Patients should be followed, even after the attacks have completely subsided, because a significant percentage will develop chronic open-angle glaucoma.

1. **Presentation** is with mild discomfort, haloes around lights and slight blurring of vision.
2. **Slit-lamp biomicroscopy** shows corneal epithelial oedema due to a high IOP (40–80 mmHg), a few aqueous cells and fine white central keratic precipitates (Fig. 9.93).
3. **Gonioscopy** shows an open angle. Unless it is performed the condition may be confused with acute primary angle-closure glaucoma. The absence of PAS helps in the differentiation from other inflammatory glaucomas.
4. **Treatment** is with topical steroids to control the inflammation and aqueous suppressants for the raised IOP. Oral non-steroidal anti-inflammatory agents may also be beneficial.



Fig. 9.93
Corneal epithelial oedema and fine keratic precipitates in the Posner–Schlossman syndrome

Lens-related glaucoma

Phacolytic glaucoma

1. **Pathogenesis**. Phacolytic glaucoma (lens protein glaucoma) is a secondary open-angle glaucoma, occurring in association with a hypermature cataract. It is more common in underdeveloped countries where patients with cataract often present late. Trabecular obstruction is caused by high-molecular-weight lens proteins which have leaked through the intact capsule into the aqueous humour. Lens protein-laden macrophages may also contribute to trabecular blockage (Fig. 9.94).

> *NB:* This condition must not be confused with phacoanaphylactic (phacoantigenic) uveitis, which is an autoimmune granulomatous reaction to lens proteins occurring in an eye with a ruptured capsule.

2. **Slit-lamp biomicroscopy**
   - The cornea may be oedematous.

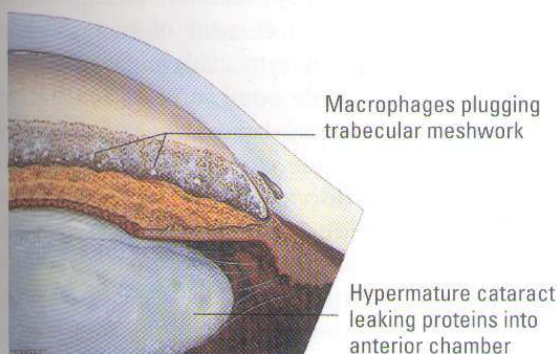


Fig. 9.94
Pathogenesis of phacolytic glaucoma



Fig. 9.95
Hypermature cataract and aqueous particles in phacolytic glaucoma

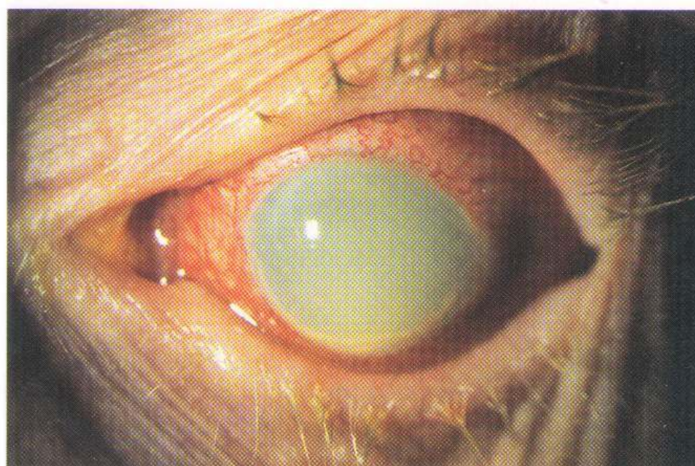


Fig. 9.96
Pseudohypopyon in phacolytic glaucoma

   - The anterior chamber is deep and the aqueous manifests floating white particles (Fig. 9.95), which may form a pseudohypopyon if very dense (Fig. 9.96).
   - A hypermature cataract is seen.
3. **Gonioscopy** shows an open angle.
4. **Treatment**, once the IOP is controlled medically, involves flushing out of proteinaceous material and cataract surgery.

> *NB:* Care must be taken not to rupture the zonules when performing anterior capsulotomy.

Phacomorphic glaucoma

1. **Pathogenesis**. Phacomorphic glaucoma is an acute secondary angle-closure glaucoma precipitated by an intumescent cataractous lens. A history of gradual impairment of vision or an increase in myopia may be obtained. The crystalline lens continues to grow throughout life. Equatorial growth (which slackens the suspensory ligament, thus



Fig. 9.97
Corneal oedema, shallow anterior chamber, dilated pupil and intumescent cataract in phacomorphic glaucoma

allowing the lens to move anteriorly) combines with antero-posterior growth to increase iridolenticular contact and potentiate pupillary block and iris bombé. Phacomorphic glaucoma and PACG therefore conceptually overlap; it may be difficult to distinguish the two in a clinical setting.

2. **Presentation** is similar to acute PACG with a shallow anterior chamber and dilated pupil (Fig. 9.97). A lens opacity is usually evident.

> *NB:* Examination of the fellow eye may demonstrate a deep anterior chamber and an open angle, thus excluding the diagnosis of PACG. Axial length measurement and records of the refraction may also be helpful in distinguishing between the two conditions.

3. **Treatment** is initially similar to acute PACG. Laser iridotomy is performed once the IOP is controlled. Cataract surgery is performed once the eye is quiet but is associated with an increased risk of capsular rupture and vitreous loss.

Traumatic glaucoma

Red cell glaucoma

Pathogenesis

A traumatic hyphaema may be associated with elevation of IOP due to trabecular blockage by red blood cells. Pupillary occlusion by a blood clot may superimpose an angle-closure component. Secondary haemorrhage, often more severe than the primary bleed, may develop within 3–5 days of the initial injury, more commonly in black people. Patients with sickle-cell haemoglobinopathies are at increased risk of developing complications associated with traumatic hyphaema.

Risk of glaucoma

Although most traumatic hyphaemas are relatively innocuous and transient, severe and prolonged elevation of IOP may damage the optic nerve and cause blood staining of the cornea. The latter can progress very rapidly and may take years to clear. The optic nerve is endangered by IOP > 50 mmHg for 2 days. The size of a hyphaema is a useful indicator of visual prognosis and risk of complications:

- Hyphaema involving less than half the anterior chamber is associated with a 4% incidence of raised IOP, a 22% incidence of complications and a final visual acuity of >6/18 in 78% of eyes.
- Hyphaema involving more than half the anterior chamber (Fig. 9.98) is associated with an 85% incidence of raised IOP, 78% incidence of complications and a final visual acuity of >6/18 in only 28% of eyes.

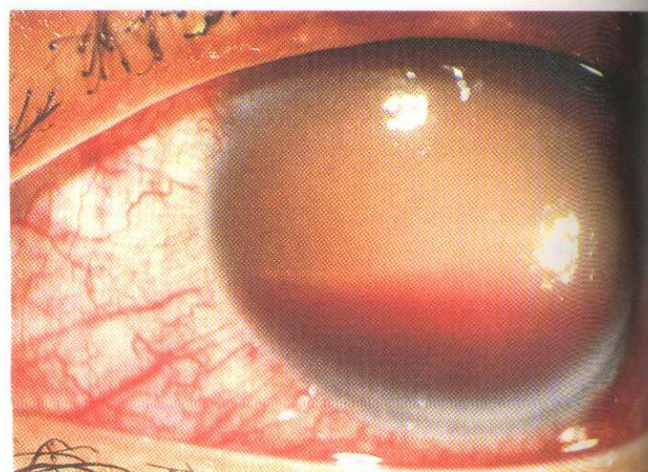


Fig. 9.98
Large hyphaema

Treatment of secondary glaucoma

Hospital admission is required for large hyphaemas.

1. **Medical**
   - Beta-blockers and/or systemic carbonic anhydrase inhibitors depending on the level of IOP. Miotics should be avoided as they may increase pupil block.
   - Topical steroids and mydriatics are useful, since there is often a superimposed element of traumatic anterior uveitis. It is preferable to achieve constant mydriasis rather than a mobile pupil in order to minimize the chances of secondary haemorrhage from the iris or ciliary body.
2. **Surgical evacuation** of the blood with or without trabeculectomy is indicated in the following circumstances:
   - An IOP of >50 mmHg for 2 days or >35 mmHg for 7 days.
   - Early corneal blood staining because it can progress to a dense opacity within a few hours.
   - Total hyphaema for more than 5 days to prevent the development of peripheral anterior synechiae and chronic secondary glaucoma.

Angle recession glaucoma

Pathogenesis

Angle recession involves rupture of the face of the ciliary body, the portion that lies between the iris root and the scleral spur, due to blunt trauma, and is detected gonioscopically as an irregular widening of the ciliary body band. Although a large percentage of eyes with traumatic hyphaema exhibit some degree of angle recession, only 6–9% develop glaucoma after 10 years. It is thought that the rise in IOP is secondary to trabecular damage rather than from angle recession itself. However, the risk of glaucoma is directly related to the extent of angle recession. Since glaucoma may not develop until months or even years after the initial injury, angle recession mandates periodic review.



Fig. 9.99
Angle recession with irregular widening of the ciliary body band (Courtesy of J. Salmon)

Clinical features

1. **Presentation** is at any age with unilateral chronic glaucoma. The diagnosis may be easily missed unless a careful past history is taken and gonioscopy performed.
2. **Slit-lamp biomicroscopy** shows signs of previous blunt trauma (see Chapter 19).
3. **Gonioscopy** may show an irregular, scarred and recessed angle with pigment within the recess (Fig. 9.99). In long-standing cases, the cleft may be obscured by fibrosis. On cursory examination, hyperpigmentation in the angle may be mistaken for pigmentary glaucoma, particularly if the corneal endothelium is also covered by pigment granules.

NB: It is important to compare the angle appearance in the two eyes and also to compare different parts of the angle in the same eye.

Treatment

1. **Medical** treatment is as for other types of secondary open-angle glaucoma but is frequently unsatisfactory (laser trabeculoplasty is ineffective).
2. **Trabeculectomy** with adjunctive antimetabolite therapy is the most effective surgical procedure.
3. **An artificial filtering shunt** should be considered if trabeculectomy fails.

Iridocorneal endothelial syndrome

The iridocorneal endothelial (ICE) syndrome typically affects one eye of a young to middle-aged woman. It consists of the following three very rare and frequently overlapping disorders: (a) *progressive iris atrophy*, (b) *iris naevus (Cogan–Reese) syndrome* and (c) *Chandler syndrome*.

Pathogenesis

The common link between the three variants of the ICE syndrome is an abnormal corneal endothelial cell layer which has the capacity to proliferate and migrate across the angle and onto the surface of the iris. The term 'proliferative endotheliopathy' has therefore been suggested to describe this disorder. The ICE syndrome may progress to glaucoma, corneal decompensation or both. Glaucoma is due to synechial angle closure secondary to contraction of this abnormal tissue. Polymerase chain reaction shows the presence of herpes simplex virus DNA in a substantial percentage of ICE syndrome corneal specimens, suggesting that the condition may be of viral origin.

General features

1. **Slit-lamp biomicroscopy**
   - Corectopia (malposition of the pupil) (Fig. 9.100).
   - Pseudopolycoria (supernumerary false pupils) in a previously normal iris (Fig. 9.101).
   - Iris atrophy of varying severity (Fig. 9.102).

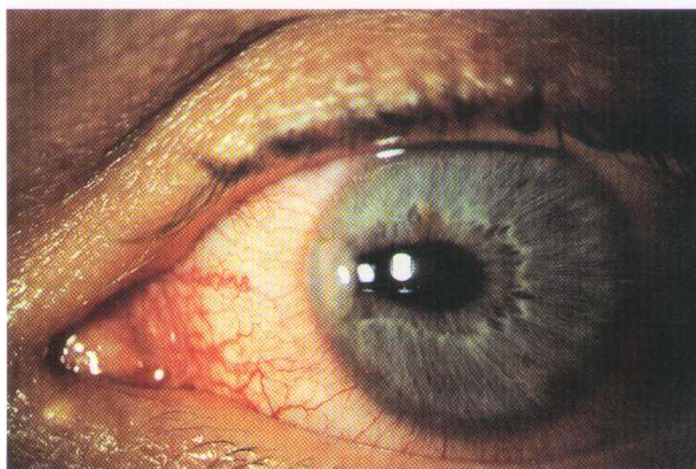


Fig. 9.100
Displacement of the pupil (corectopia) towards the site of peripheral anterior synechiae in ICE



Fig. 9.101
Supernumerary false pupil (pseudopolycoria) in ICE

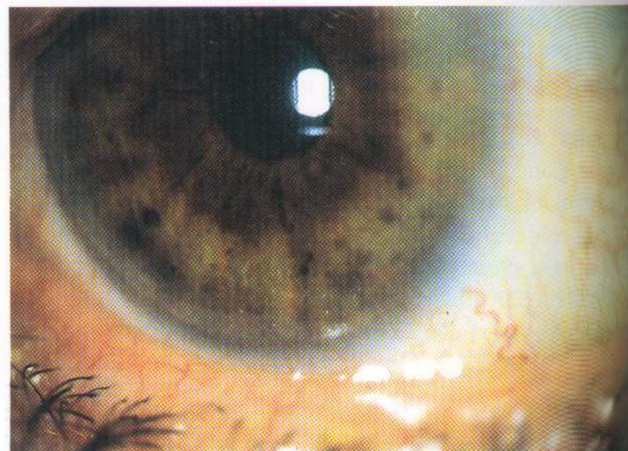

Fig. 9.102
Stromal iris atrophy in ICE


Fig. 9.103
'Hammered-silver' endothelial changes in ICE


Fig. 9.104
Peripheral anterior synechiae in ICE


Fig. 9.105
Progressive iris atrophy


Fig. 9.106
Advanced progressive iris atrophy


Fig. 9.107
Pigmented iris nodules in the Cogan–Reese syndrome

- Corneal endothelial abnormalities characterized by a 'hammered-silver' appearance similar to Fuchs dystrophy when viewed in specular reflected light (Fig. 9.103). Corneal oedema secondary to endothelial decompensation is present in more advanced cases.

2. **Gonioscopy** shows broad-based peripheral anterior synechiae that often extend anterior to Schwalbe line (Fig. 9.104).
3. **Glaucoma** is present in about 50% of cases.

Specific features

In their purest form, the three conditions are easily distinguished from each other. However, there is frequently considerable overlap and clear differentiation may be difficult. Occasionally, during follow-up one condition can be observed changing into another. The differentiation depends primarily on the iris changes.

1. **Progressive iris atrophy** is characterized by severe iris changes with stromal atrophy, hole formation and marked displacement of the pupil towards areas of PAS (Figs 9.105 and 9.106). In between areas of atrophy the stroma appears normal.
2. **The iris naevus (Cogan–Reese) syndrome** is characterized by either a diffuse naevus which covers the anterior iris or by pigmented, pedunculated iris nodules (Fig. 9.107). The pattern of the iris surface appears smudged and matted. Iris atrophy is absent in 50% of cases and in the remainder it is usually mild to moderate although corectopia may be severe.

> *NB:* It is important not to misdiagnose a diffuse iris melanoma as the iris naevus syndrome.

3. **Chandler syndrome** is characterized by severe corneal changes and frequently presents with blurred vision and haloes due to corneal oedema. Stromal atrophy is absent in about 60% of cases and in the remainder is variable in its severity; corectopia is mild to moderate. Glaucoma is usually less severe than in the other two syndromes, and at presentation the IOP may be normal.

Treatment of glaucoma

1. **Medical** treatment is often ineffective.
2. **Trabeculectomy**, even when combined with adjunctive antimetabolite therapy, is frequently unsuccessful because of late-onset bleb failure.
3. **Artificial filtering shunts** are eventually required in many cases.

Miscellaneous secondary glaucomas

Ghost cell glaucoma

1. **Pathogenesis**. Ghost cell glaucoma is due to trabecular obstruction by degenerate erythrocytes. About 2 weeks after vitreous haemorrhage, haemoglobin leaks from the erythrocytes, which evolve into 'ghost' cells, which then pass through a defect in the anterior hyaloid face into the anterior chamber. Because their pliability is lost, the cells become entrapped within the pores of the trabeculum and obstruct aqueous outflow. Ghost cell glaucoma may occur in the following settings:



Fig. 9.108
Ghost cell glaucoma

- Cataract surgery in the context of pre-existing vitreous haemorrhage.
- Vitreous haemorrhage in an already aphakic or pseudophakic eye.
- When cataract surgery is complicated by a vitreous haemorrhage and hyphaema. The hyphaema clears, but the red cells in the vitreous persist and evolve into ghost cells.

2. **Clinical features**
   - The cornea may be oedematous due to elevated IOP or surgical trauma.
   - The anterior chamber exhibits ghost cells, which may be recognized as reddish-brown or khaki particles in the aqueous (Fig. 9.108). They should not be confused with leucocytes, since this may result in unwarranted therapy for uveitis.
3. **Treatment**
   a. ***Medical*** treatment with aqueous suppressants.
   b. ***Irrigation*** of the anterior chamber with washing out of the ghost cells if medical therapy fails.
   c. ***Pars plana vitrectomy*** may occasionally be required for persistent vitreous haemorrhage.

Glaucoma in carotid–cavernous fistula

An arteriovenous fistula is an abnormal communication between a previously normal vein and an artery. The blood within the affected vein becomes 'arterialized', and the intravenous pressure rises so that venous blood flow may become altered both in rate and direction. The clinical features of an arteriovenous fistula are largely due to these altered vascular dynamics with subsequent reduction of arterial perfusion, ocular hypoxia and venous congestion (*see* Chapter 17).

1. **Pathogenesis of glaucoma**
   - Secondary open-angle glaucoma due to raised episcleral venous pressure, in turn resulting from a generalized increase in orbital venous pressure, is the most common clinical picture. Gonioscopy may show blood in Schlemm canal.

- Neovascular glaucoma as a result of anterior segment ischaemia.
- Secondary angle closure due to congestion of the uveal tract as a result of increased pressure in the vortex veins (*see* later).

2. **Clinical features.** In patients with large carotid–cavernous fistulae, the other features tend to overshadow the elevation of IOP. However, some patients with relatively mild fistulae, particularly of the indirect type (dural shunt), may present with unilateral glaucoma and congestion of the globe, and the possibility of an underlying carotid–cavernous fistula may be overlooked.
3. **Treatment** is aimed at controlling the IOP medically until the shunt resolves or is treated.

Glaucoma in intraocular tumours

Approximately 5% of eyes with intraocular tumours develop a secondary elevation of IOP. Depending on the location of the tumour one or more of the following mechanisms may be responsible:

1. **Trabecular block**
   - Solid tumour invasion in which the trabeculum is directly invaded by neoplastic cells originating from either a primary melanoma or a metastatic tumour of the anterior uvea. Rarely tumour seeding from a retinoblastoma may also invade the trabeculum.
   - Melanomalytic glaucoma may occur in some eyes with iris melanoma; it is due to trabecular blockage by macrophages which have ingested pigment and tumour cells, similar to phacolytic glaucoma.
2. **Secondary angle closure**
   - Neovascular glaucoma is the most common mechanism in eyes with choroidal melanoma or retinoblastoma.
   - Anterior displacement of the iris–lens diaphragm may occur in an eye with a ciliary body melanoma or a large tumour of the posterior segment.

Glaucoma in ciliochoroidal detachment

1. **Pathogenesis of glaucoma.** Ciliary body detachment with forward rotation around the scleral spur leads to anterior displacement of the iris–lens diaphragm. The anterior chamber shallows, resulting in appositional angle closure without iris bombé.
2. **Causes of ciliochoroidal detachment**
   a. Postoperative
   - Choroidal congestion from an over-tight scleral buckle for retinal detachment.
   - Aggressive panretinal photocoagulation causing inflammatory choroidal exudation.
   - Suprachoroidal haemorrhage following intraocular surgery.
   - After trabeculectomy, especially if there is bleb leakage. The globe is initially hypotonous; later the IOP starts to rise.

   b. Inflammatory causes include scleritis and Harada disease.
   c. Vascular causes include arteriovenous malformation, nanophthalmos and after central retinal vein occlusion.
   d. Uveal effusion syndrome
3. **Signs**
   - Extremely shallow anterior chamber, which is flat peripherally, but without iris bombé.
   - Closed angle.
   - Choroidal detachment.
4. **Treatment**
   a. Medical treatment with mydriatics, topical steroids and aqueous suppressants.
   b. Laser peripheral iridoplasty (gonioplasty), not iridotomy.
   c. Surgery involves repairing a leaking trabeculectomy bleb, cutting an over-tight encircling band and, as a last resort, drainage of choroidal detachment.

Glaucoma in epithelial ingrowth

1. **Pathogenesis.** Epithelial ingrowth is a rare complication of anterior segment surgery or trauma. Conjunctival or corneal epithelial cells migrate through the wound and proliferate in the anterior segment, in a cystic or diffuse manner. The latter is characterized by the proliferation of sheets of epithelial cells over the posterior cornea, trabeculum, iris and ciliary body, and is more commonly associated with secondary glaucoma than the cystic variety. Elevation of IOP is a combination of often pre-existing peripheral anterior synechiae, destruction of the trabeculum by the epithelial membrane, and/or obstruction of the trabeculum by desquamated epithelial cells and associated inflammatory cells.
2. **Clinical features**
   - Persistent postoperative anterior uveitis.
   - Diffuse epithelialization is characterized by a translucent membrane with scalloped border involving the posterior corneal surface (Fig. 9.109) and anterior vitreous face in the sector of the incision.
   - Pupillary distortion.



Fig. 9.109
Diffuse epithelial ingrowth

3. **Treatment** of this potentially blinding condition is aimed at eradicating the invading epithelium to avoid recurrence or the conversion of epithelial cysts into diffuse epithelialization with consequent intractable glaucoma.
   a. ***Block excision*** involves simultaneous excision of adjacent iris, pars plicata of the ciliary body, together with all layers of the sclera and cornea in contact with the lesion. The resultant defect is covered with a tectonic corneoscleral graft. The area of iris involvement may be identified by applying argon laser burns which will cause whitening of the affected area.
   b. ***Cryotherapy*** may be applied trans-sclerally to devitalize the epithelium remaining on the posterior surface of the cornea, in the angle and on the ciliary body. Intraocular air is used to insulate other tissues from the effects of the cryotherapy.
   c. ***Artificial filtering shunts*** are of value for medically uncontrolled glaucoma associated with extensive epithelial ingrowth unsuitable for surgical excision.

Glaucoma in iridoschisis

Iridoschisis is a rare condition which typically affects the elderly and is often bilateral. It is associated with underlying angle-closure glaucoma in 90% of cases. It is thought that acute or intermittent angle closure results in iris atrophy because of high IOP.



Fig. 9.110
Shallow anterior chamber in iridoschisis

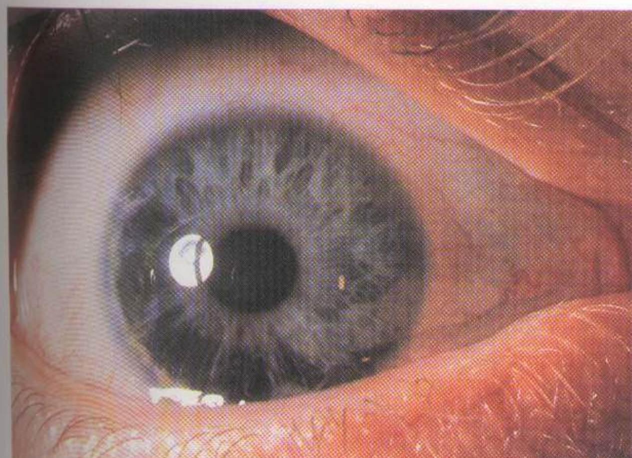


Fig. 9.111
Mild iridoschisis

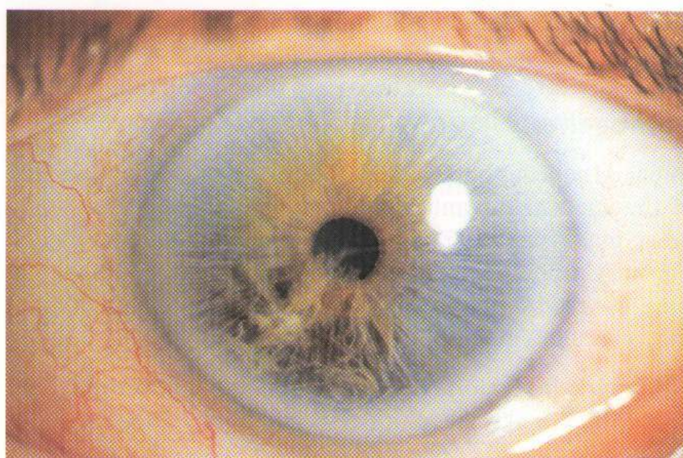


Fig. 9.112
Splitting of the anterior leaf of the iris in iridoschisis

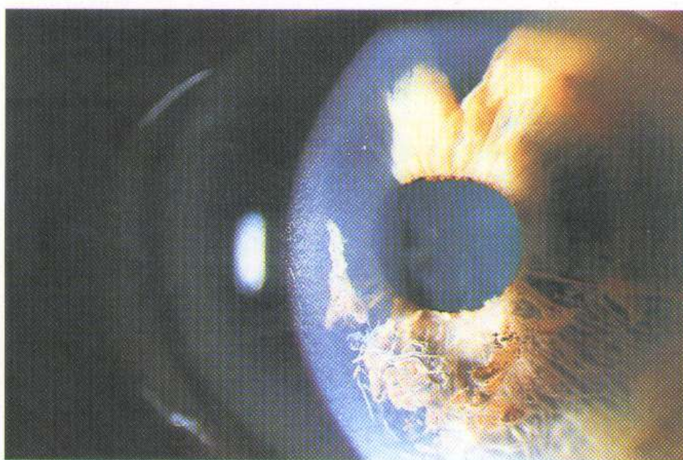


Fig. 9.113
Severe iridoschisis with disintegration of iris fibrils

1. **Clinical features**
   - Shallow anterior chamber (Fig. 9.110).
   - Iridoschisis usually involves the inferior iris. The severity ranges from intrastromal atrophy (Fig. 9.111) to extensive splitting of the anterior leaf (Fig. 9.112) and disintegrated iris fibrils (Fig. 9.113) which may float in the anterior chamber.
   - Gonioscopy shows a narrow occludable angle which may be associated with peripheral anterior synechiae.
2. **Treatment** initially involves peripheral laser iridotomy. Subsequent treatment is aimed at limiting glaucomatous damage.

Primary congenital glaucoma

Although primary congenital glaucoma (PCG) is the most common of the congenital glaucomas, it is still a very rare condition, affecting 1:10,000 births; 65% of patients are boys.

Most cases of PCG are sporadic. In approximately 10% inheritance is autosomal recessive with incomplete penetrance.

Pathogenesis

Impaired aqueous outflow in PCG is caused by maldevelopment of the angle of the anterior chamber, unassociated with any other major ocular anomalies (isolated trabeculodysgenesis). Clinically, trabeculodysgenesis is characterized by absence of the angle recess with the iris inserted directly into the surface of the trabeculum in one of two configurations:

1. **Flat iris insertion**. The iris inserts flatly and abruptly into the thickened trabeculum at or anterior to the scleral spur (Fig. 9.114a).
2. **Concave iris insertion** is less common. The superficial iris tissue sweeps over the iridotrabecular junction and the trabeculum (Fig. 9.114b). In contrast to a flat iris insertion, the angular structures are obscured by the overlying iris tissue, which is either sheet-like or consists of a dense arborizing meshwork.

Classification

1. **True congenital glaucoma** (40%) in which IOP becomes elevated during intrauterine life.
2. **Infantile glaucoma** (55% of cases) which manifests prior to the third birthday.
3. **Juvenile glaucoma**, the least common, in which the pressure rise develops after the third birthday but before the age of 16 years. This condition may simulate POAG. Gonioscopy is normal or reveals trabeculodysgenesis.

Clinical features

These depend on the age of onset and the level of IOP. Both eyes are affected in 75% of cases although involvement is frequently asymmetrical.

1. **Corneal haze** is often the first sign noticed by the parents (Fig. 9.115). It is caused by epithelial and stromal oedema secondary to raised IOP and may be associated with lacrimation, photophobia and blepharospasm.
2. **Buphthalmos** is a large eye as a result of stretching due to elevated IOP prior to the age of 3 years (Fig. 9.116). It is not usually reported by the parents unless unilateral and advanced. As the sclera stretches it becomes thinner and translucent; the eye then takes on a blue appearance due to enhanced visualization of the underlying uvea. As ocular enlargement continues the anterior chamber deepens; in advanced cases, the zonular fibres stretch and the lens may rarely subluxate. The increased axial length also causes axial myopia, which may give rise to anisometropic amblyopia.

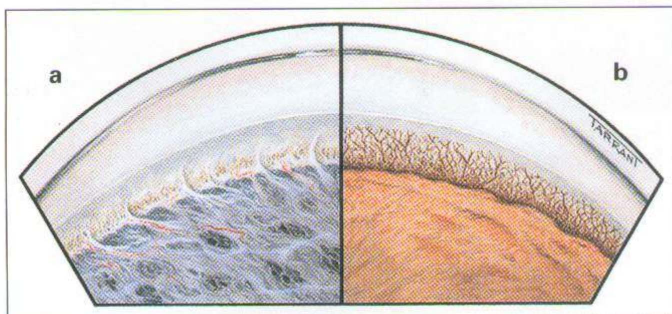


Fig. 9.114
Trabeculodysgenesis in primary congenital glaucoma. (**a**) Flat anterior iris insertion; (**b**) concave iris insertion



Fig. 9.115
Cloudy cornea in congenital glaucoma



Fig. 9.116
Bilateral buphthalmos involving the right eye more than the left

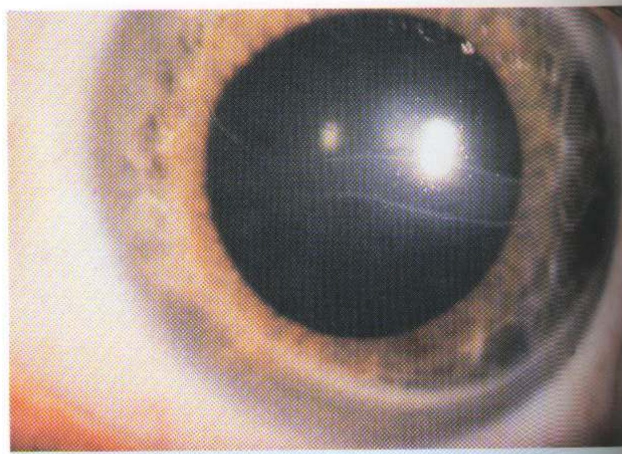


Fig. 9.117
Haab striae

3. **Breaks in Descemet membrane** (Fig. 9.117) secondary to corneal stretching may be associated with a sudden influx of aqueous into the corneal stroma. Chronic stromal oedema may lead to permanent scarring. Haab striae represent healed breaks in Descemet membrane and appear as horizontal curvilinear lines.
4. **Optic disc cupping** in infants may regress once the IOP is normalized. Most normal infants exhibit no apparent cup; very few have a cup–disc ratio greater than 0.3, unlike a high percentage of infants with PCG. In contrast to the adult eye, the scleral canal in the infant eye enlarges as part of the generalized enlargement of the globe and the lamina cribrosa may bow posteriorly, in response to elevated IOP. Cup size may therefore be increased from neuronal loss, enlargement of the scleral canal, or both.

Differential diagnosis

1. **Cloudy cornea at birth**
   - Birth trauma may give rise to corneal oedema due to breaks in Descemet membrane.
   - Intrauterine rubella may give rise to a cloudy cornea due to keratitis.

> *NB:* Ten per cent of infants with the rubella syndrome also have congenital glaucoma due to an angle anomaly similar to that in PCG. This may be missed because the eye may not appear significantly enlarged, due to pre-existing microphthalmos.

   - Metabolic disorders such as mucopolysaccharidoses and mucolipidoses.
   - Congenital hereditary endothelial dystrophy (*see* Chapter 5).
2. **Large cornea** due to megalocornea or very high myopia.
3. **Lacrimation** resulting from delayed canalization of the nasolacrimal duct.
4. **Secondary infantile glaucoma**
   - Tumours such as retinoblastoma and juvenile xanthogranuloma.
   - Persistent hyperplastic primary vitreous.
   - Retinopathy of prematurity.
   - Intraocular inflammation.
   - Trauma.
   - Ectopia lentis.

Initial evaluation

This should be performed under general anaesthesia with intravenous ketamine, since other agents may lower IOP. Examination of the optic discs should be undertaken first, followed by measurement of IOP and corneal diameters, and finally gonioscopy.

1. **The IOP** is measured with the Perkins tonometer or Tono-Pen.
2. **The corneal diameter** is measured in both vertical and horizontal meridians with callipers. A diameter > 11 mm prior to the age of 1 year or > 13 mm at any age should be viewed with suspicion. Diameters of 14 mm are typical of advanced buphthalmos.
3. **Gonioscopy** should be performed with a Koeppe lens or one of the other direct goniolenses.

Surgery

1. **Goniotomy** (Fig. 9.118) is performed at the initial examination if the diagnosis is confirmed, provided there is sufficient corneal clarity and the angle can be visualized. Although this procedure may need to be repeated the eventual success rate is about 85%. Goniotomy is unlikely to

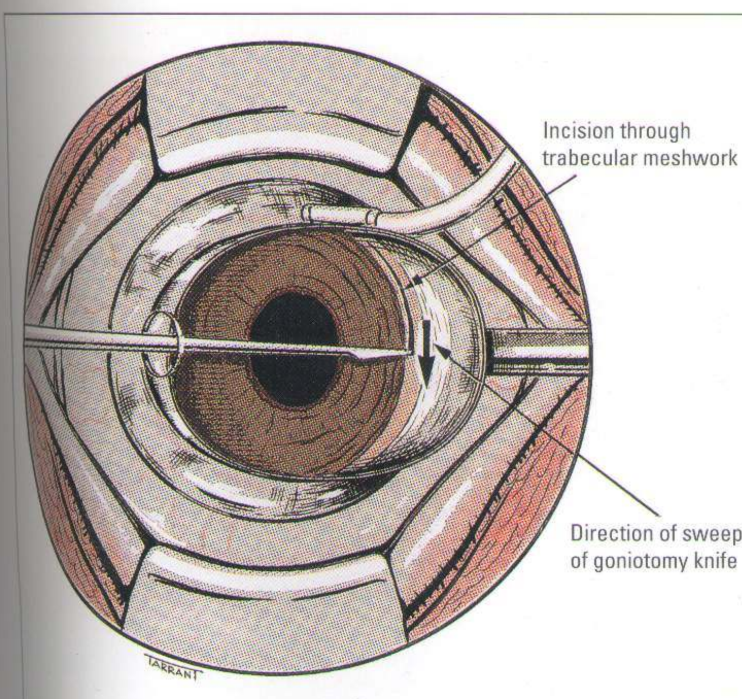


Fig. 9.118
Goniotomy. A circumferential incision is made in the trabecular meshwork

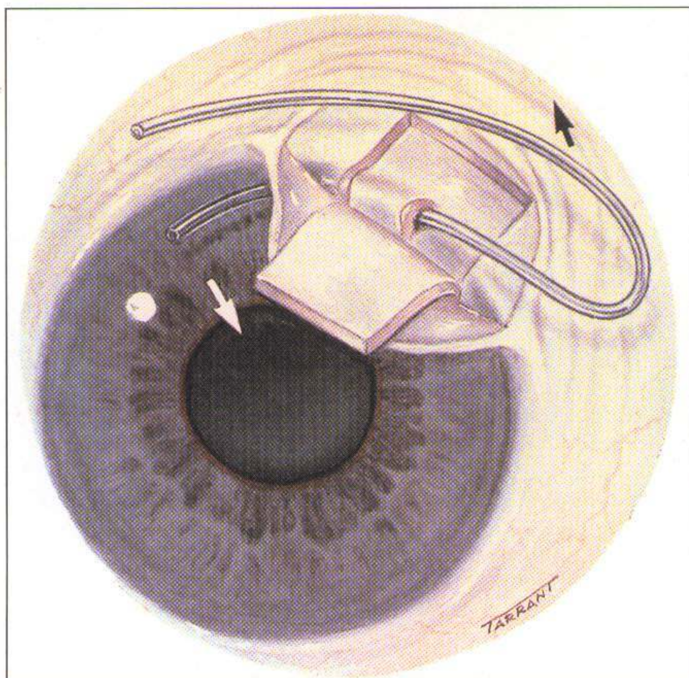


Fig. 9.119
Trabeculotomy. A trabeculotome is inserted into Schlemm canal and rotated into the anterior chamber

be effective if corneal diameter equals or exceeds 14 mm, since in such eyes the canal of Schlemm is obliterated.

2. **Trabeculotomy** (Fig. 9.119) may be necessary if corneal clouding prevents visualization of the angle or when repeated goniotomy has failed.
3. **Trabeculectomy** is often successful, particularly when combined with trabeculotomy and adjunctive antimetabolites.

Follow-up

Patients should be reviewed 1 month after initial surgery. The IOP and corneal diameters should be monitored at regular intervals because progressive enlargement of the corneal diameter is as important a sign of uncontrolled congenital glaucoma as progressive visual field loss in adult glaucoma. About 50% of patients suffer visual loss from optic nerve damage, anisometropic amblyopia, corneal scarring, cataract and lens subluxation. A buphthalmic eye is also susceptible to traumatic damage.

Iridocorneal dysgenesis

Iridocorneal dysgenesis consists of the following overlapping rare congenital disorders involving the cornea and iris, some of which may be associated with glaucoma. These conditions occur as a result of abnormal neural crest cell development and are: (a) *Axenfeld–Rieger syndrome*, (b) *Peters anomaly* and (c) *aniridia*.

Axenfeld–Rieger syndrome

Axenfeld–Rieger syndrome is a spectrum of rare developmental disorders, designated in current nomenclature by the following eponyms:

Axenfeld anomaly

1. **Gonioscopy** shows a prominent and anteriorly displaced Schwalbe line (posterior embryotoxon) (Fig. 9.120) onto which are attached strands of peripheral iris tissue (Fig. 9.121).
2. **Glaucoma** is rare.

Rieger anomaly

This is an AD condition with a high degree of penetrance. Involvement is usually bilateral but not always symmetrical.

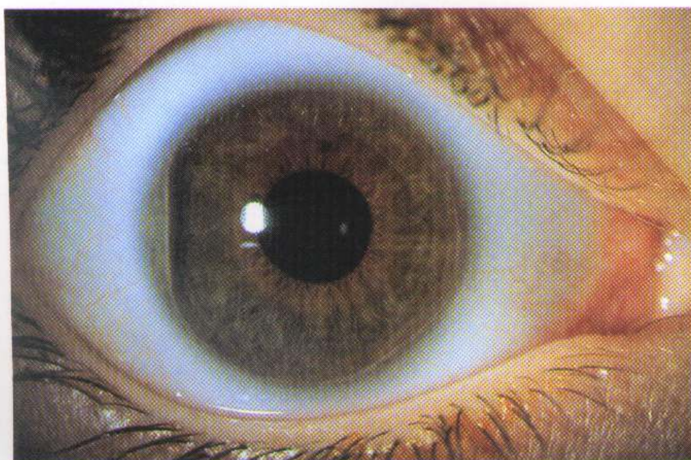


Fig. 9.120
Posterior embryotoxon, most marked temporally where Descemet membrane is partially detached

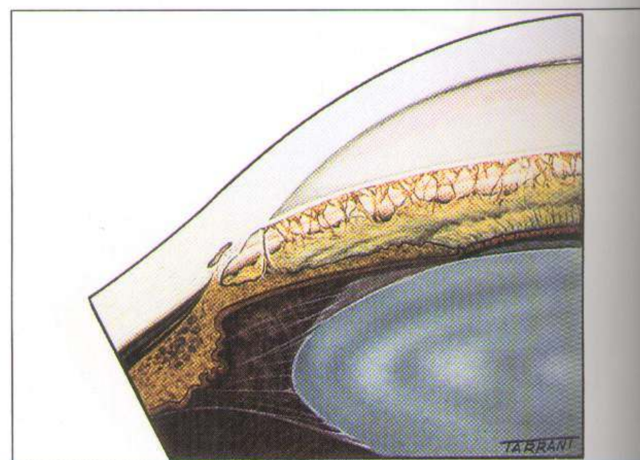


Fig. 9.121
Gonioscopic appearance of Axenfeld anomaly showing strands of peripheral iris attached to a posterior embryotoxon

1. **Slit-lamp biomicroscopy**
   - Posterior embryotoxon.
   - Schwalbe line may become detached into the anterior chamber.
   - Iris stromal hypoplasia (Fig. 9.122), corectopia (Fig. 9.123), pseudopolycoria (Fig. 9.124) and ectropion uveae (Fig. 9.125).
2. **Gonioscopy** in mild cases shows Axenfeld anomaly. In severe cases, broad leaves of the iris stroma adhere to the cornea anterior to Schwalbe line (Fig. 9.126).
3. **Glaucoma** develops in about 50% of cases, usually during early childhood or early adulthood, due to an associated angle anomaly or secondary synechial angle closure. The elevation of IOP should be initially managed medically, although surgery may be required.

Rieger syndrome

This is linked to the region of the epidermal growth factor gene on chromosome 4. It is characterized by Rieger anomaly in association with the following extraocular malformations:

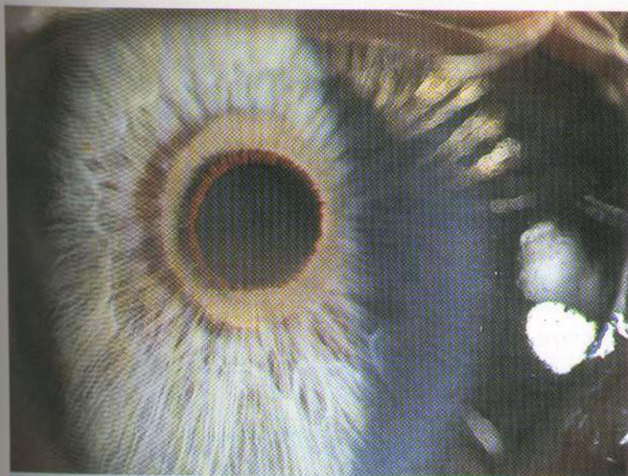


Fig. 9.122
Stromal iris hypoplasia in Rieger anomaly

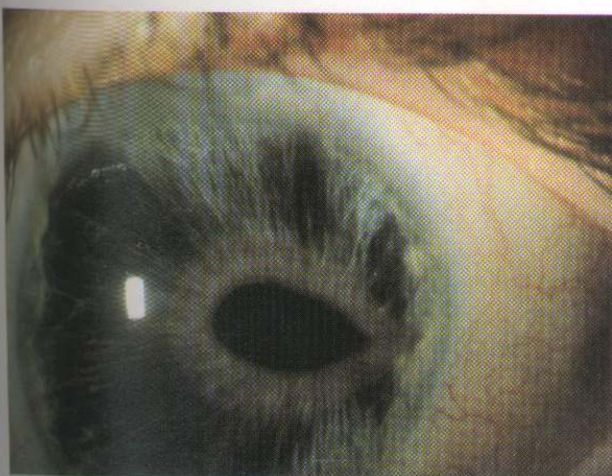


Fig. 9.123
Corectopia and stromal iris hypoplasia in Rieger anomaly

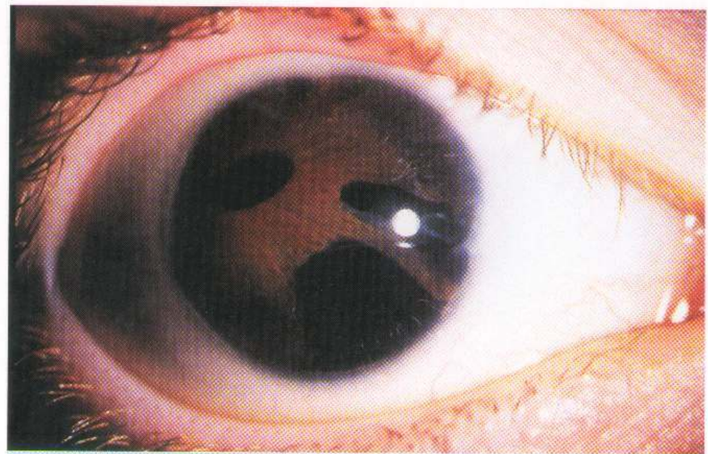


Fig. 9.124
Corectopia and full-thickness iris defects in Rieger anomaly

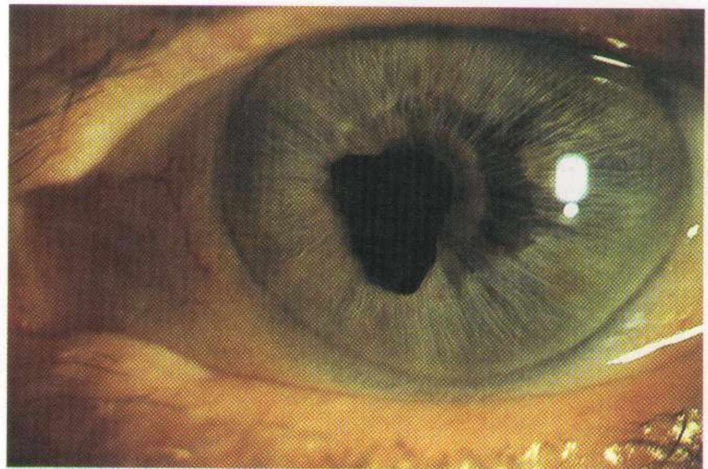


Fig. 9.125
Ectropion uveae and mild iris stromal atrophy in Rieger anomaly

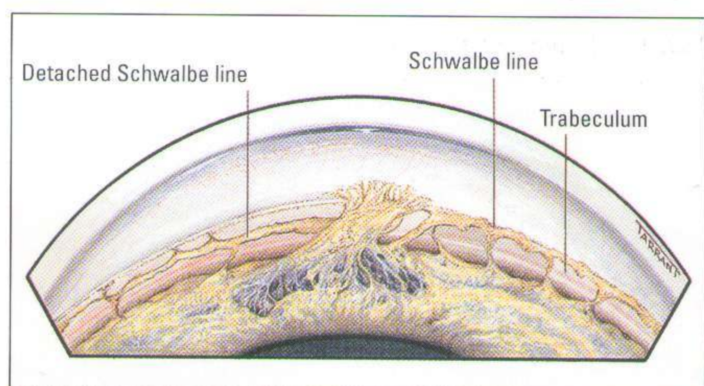


Fig. 9.126
Peripheral anterior synechiae and partial detachment of Descemet membrane in Rieger syndrome

1. **Dental** anomalies consisting of hypodontia (few teeth) and microdontia (small teeth) (Fig. 9.127).
2. **Facial** anomalies include maxillary hypoplasia, broad nasal bridge, telecanthus (increased distance between the medial canthi) and hypertelorism (increased interorbital distance).



Fig. 9.127
Dental abnormalities in Rieger syndrome (Courtesy of K. Nischal)



Fig. 9.128
Redundant paraumbilical skin in Rieger syndrome (Courtesy of K. Nischal)

3. Other anomalies include redundant paraumbilical skin (Fig. 9.128) and defects in the region of the pituitary gland.

Peters anomaly

This is an extremely rare but serious condition which is bilateral in 80% of cases. It is the result of defective neural crest cell migration in the sixth to eight weeks of fetal development, during which time the anterior segment of the eye is formed. Most cases are sporadic, although autosomal recessive inheritance and chromosomal defects have been described.



Fig. 9.129
Corneal opacity in Peters anomaly

1. Clinical features

- Corneal opacity (Fig. 9.129) of variable density, with an underlying defect involving the posterior stroma, Descemet membrane and endothelium.
- Strands of iris tissue adhere to the margin of the opacity (Figs 9.130 and 9.131a).
- In its more severe degrees the anomaly is characterized by keratolenticular adhesion (Fig. 9.132) or apposition (*see* Fig. 9.131b).



Fig. 9.130
Iridocorneal adhesions in Peters anomaly

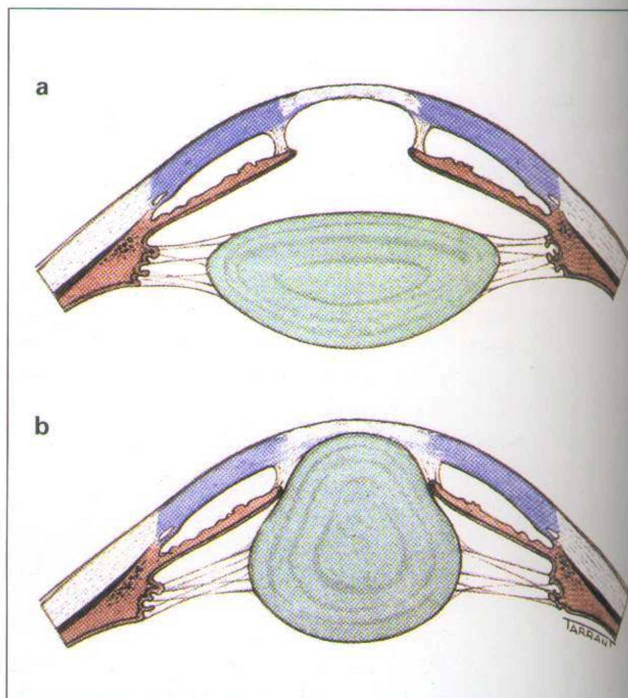


Fig. 9.131
Peters anomaly. (**a**) Iridocorneal adhesions; (**b**) keratolenticular apposition

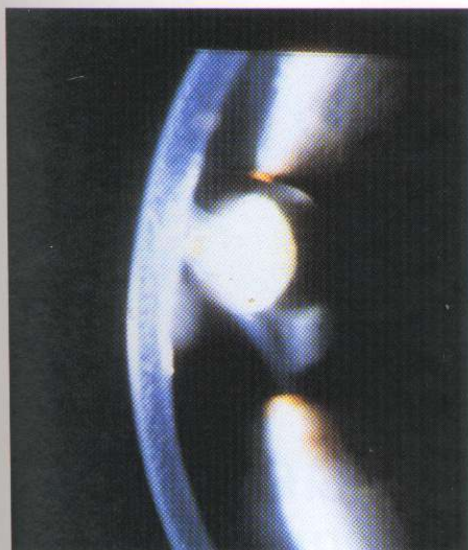


Fig. 9.132
Keratolenticular adhesion in Peters anomaly

- Miscellaneous occasional anomalies include microphthalmos, cornea plana, sclerocornea, corectopia, iris hypoplasia and anterior polar cataract.

2. **Glaucoma**, which is often congenital, occurs in about 50% of cases as a result of an associated angle anomaly.

Aniridia

Aniridia (AN) is a bilateral condition with life-threatening associations. It occurs as a result of abnormal neuroectodermal development secondary to a mutation in the *PAX6* gene linked to 11p13. This gene controls the development of a number of structures, hence the broad nature of ocular and systemic manifestations. Glaucoma is common and difficult to control.

Classification

1. **AN-1** is AD, accounts for 66% of cases and has no systemic implications. Penetrance is complete, but expressivity variable.
2. **AN-2** (Miller syndrome) is sporadic and accounts for 33%. It carries a 30% risk of Wilm tumour developing before the age of 5 years.
3. **AN-3** (Gillespie syndrome) is recessively inherited and accounts for the remainder. It is associated with mental handicap and cerebellar ataxia.

Clinical features

1. **Presentation** is typically at birth with nystagmus and photophobia. The parents may have noticed absence of irides or 'dilated pupils'.
2. **Signs**

   a. Aniridia is variable in severity, ranging from minimal (detectable only by retroillumination), to partial (Fig. 9.133) and total (Fig. 9.134). However, even eyes with 'total' involvement usually show a residual frill of iris tissue in the angle on gonioscopy (Fig. 9.135).



Fig. 9.133
Partial aniridia

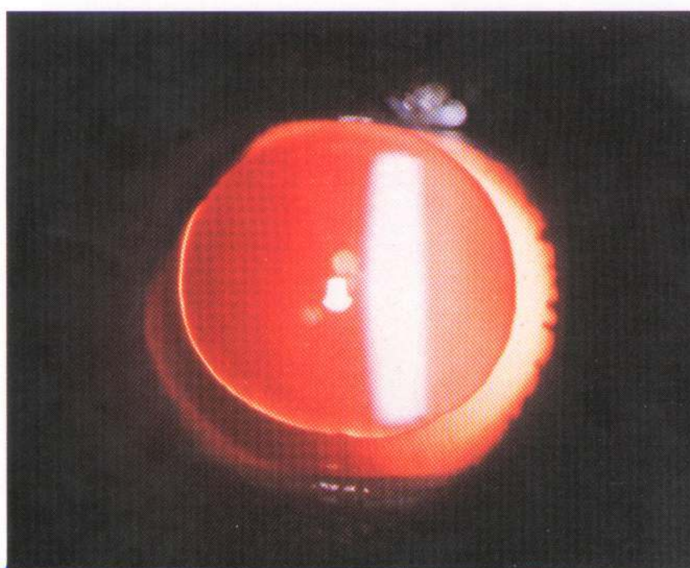


Fig. 9.134
Total aniridia

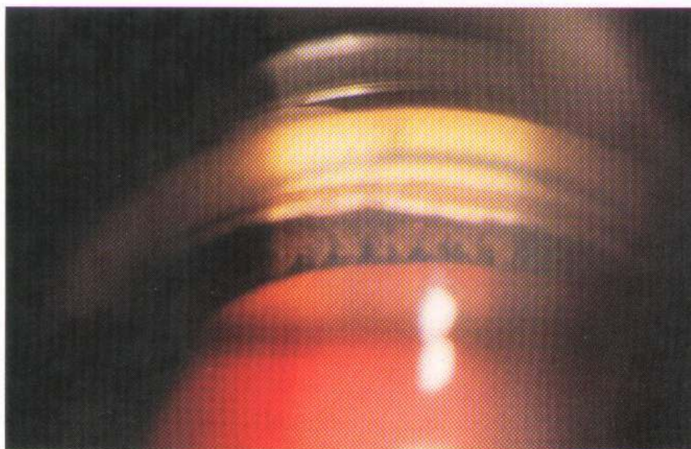


Fig. 9.135
Gonioscopic view of aniridia showing remnants of the iris root

   b. Corneal lesions include opacity, epibulbar dermoids, microcornea, sclerocornea and keratolenticular adhesions. The corneal surface often manifests epithelial



Fig. 9.136
Subluxation of a cataractous lens in aniridia

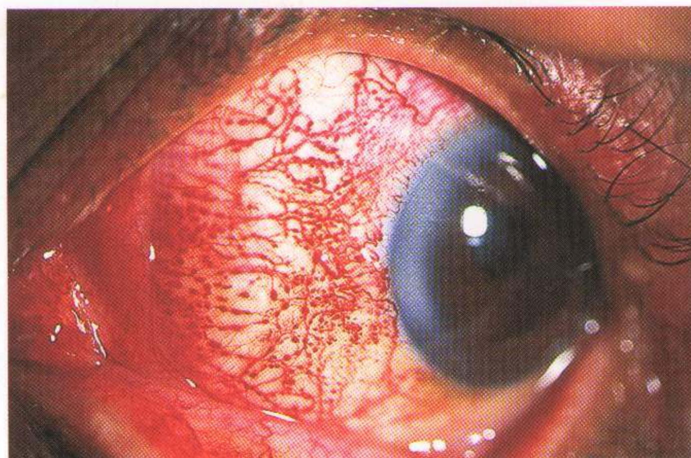


Fig. 9.137
Episcleral angioma in Sturge–Weber syndrome

defects and may become conjunctivalized as a result of limbal stem cell deficiency.

c. ***Lenticular*** changes include cataract, subluxation (usually superiorly) (Fig. 9.136), congenital aphakia and persistent pupillary membranes.

d. ***Fundus*** may exhibit foveal hypoplasia, optic disc hypoplasia and choroidal coloboma.

Management

1. **Opaque contact lenses** may be used to create an artificial pupil and improve vision and cosmesis.
2. **Topical lubricants** are frequently required for associated keratopathy.
3. **Cataract surgery** is often required. Care must be taken to minimize trauma to the limbus and preserve stem cell function.

Glaucoma

This occurs in approximately 75% of patients and usually presents in late childhood or adolescence.

1. **The mechanism** is synechial angle closure secondary to the pulling forward of rudimentary iris tissue by contraction of pre-existing fibres that bridge the angle.
2. **Treatment** is difficult and the prognosis guarded.
   a. ***Medical*** therapy is inadequate in most cases.
   b. ***Goniotomy*** may prevent subsequent rise in IOP if performed before the development of irreversible synechial angle closure.
   c. ***Artificial filtering shunts*** may be effective in established cases.
   d. ***Diode laser cycloablation*** may be necessary if other modalities fail.

Glaucoma in phacomatoses

Sturge–Weber syndrome

Sturge–Weber syndrome (encephalotrigeminal angiomatosis) is characterized by naevus flammeus and intracranial leptomeningeal angiomata (*see* Chapter 20). Glaucoma develops in about 30% of patients ipsilateral to the facial haemangioma, especially if the lesion affects the upper eyelid.

1. **The pathogenesis** of glaucoma is controversial. Isolated trabeculodysgenesis may be instrumental in the infant, whereas raised episcleral venous pressure associated with an arteriovenous communication in an episcleral angioma (Fig. 9.137) may be responsible in older patients. Often, however, the cause is obscure.
2. **Presentation** of glaucoma in 60% of patients is within the first 2 years of life with buphthalmos. The remainder manifest at any time from infancy to adulthood.
3. **Treatment**
   a. ***Medical*** treatment with topical latanoprost may be successful.
   b. ***Goniotomy*** may be successful in eyes with angle anomalies.
   c. ***Combined trabeculotomy–trabeculectomy*** gives good results in early-onset cases. The rationale is that trabeculotomy addresses the barrier to aqueous outflow posed by a congenital angle anomaly, while trabeculectomy bypasses the episcleral veins.

> ***NB:*** Surgery carries a high risk of choroidal effusion and suprachoroidal haemorrhage.

Neurofibromatosis-1

Neurofibromatosis-1 (NF-1, von Recklinghausen disease) is a disorder that primarily affects neural cell growth. Inheritance is autosomal dominant with irregular penetrance and variable expressivity (*see* Chapter 20). Glaucoma is uncommon, usually unilateral and congenital. About 50% of

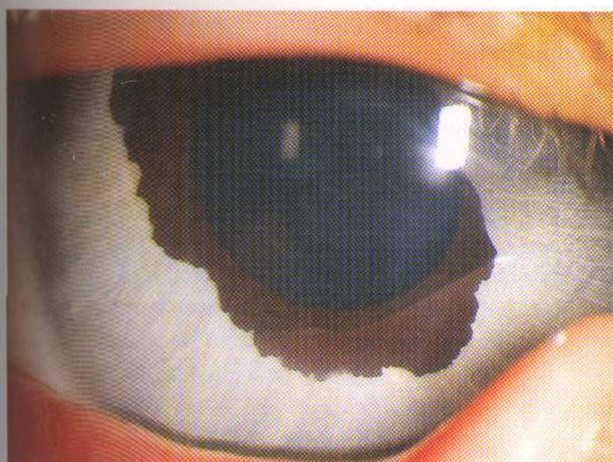


Fig. 9.138
Congenital ectropion uveae in neurofibromatosis-1

patients with glaucoma have an ipsilateral neurofibroma of the upper eyelid or exhibit facial hemiatrophy.

1. **Pathogenesis**
   - Obstruction of aqueous outflow by neurofibromatous tissue in the angle.
   - Developmental angle anomaly which may be associated with congenital ectropion uveae (Fig. 9.138).
   - Secondary angle closure caused by forward displacement of the peripheral iris associated with neurofibromatous thickening of the ciliary body.
   - Secondary synechial angle closure caused by contraction of a fibrovascular membrane.
2. **Treatment** is similar to that of primary congenital glaucoma but the prognosis is worse.

Anti-glaucoma drugs

Beta-blockers

Pharmacology

Adrenergic neurones secrete noradrenaline at sympathetic post-ganglionic nerve endings.

1. **Adrenergic receptors** are of the following four main types (Fig. 9.139):
   a. *Alpha-1* receptors are located in the arterioles, dilator pupillae and Muller muscle. Stimulation gives rise to hypertension, mydriasis and lid retraction.
   b. *Alpha-2* receptors are inhibitory receptors located in the ciliary epithelium. Stimulation results in diminished aqueous secretion. There may also be an increase in uveoscleral outflow.
   c. *Beta-1* receptors are located in heart muscle and give rise to tachycardia when stimulated.
   d. *Beta-2* receptors are located in the bronchi and ciliary epithelium ($\beta_2 > \beta_1$). Stimulation results in bronchodilation and increased aqueous production.
2. **Beta-blockers** antagonize the effects of catecholamines at beta receptors. They reduce IOP by decreasing aqueous secretion and are therefore useful in all types of glaucoma but about 10% of the population are unresponsive. Beta-blockers may be non-selective or cardioselective. Non-selective beta-blockers are equipotent at beta-1 and beta-2 receptors, while cardioselective are more potent at beta-1 receptors. The advantage, at least in theory, is that the bronchoconstrictive effect of beta-2 blockade is

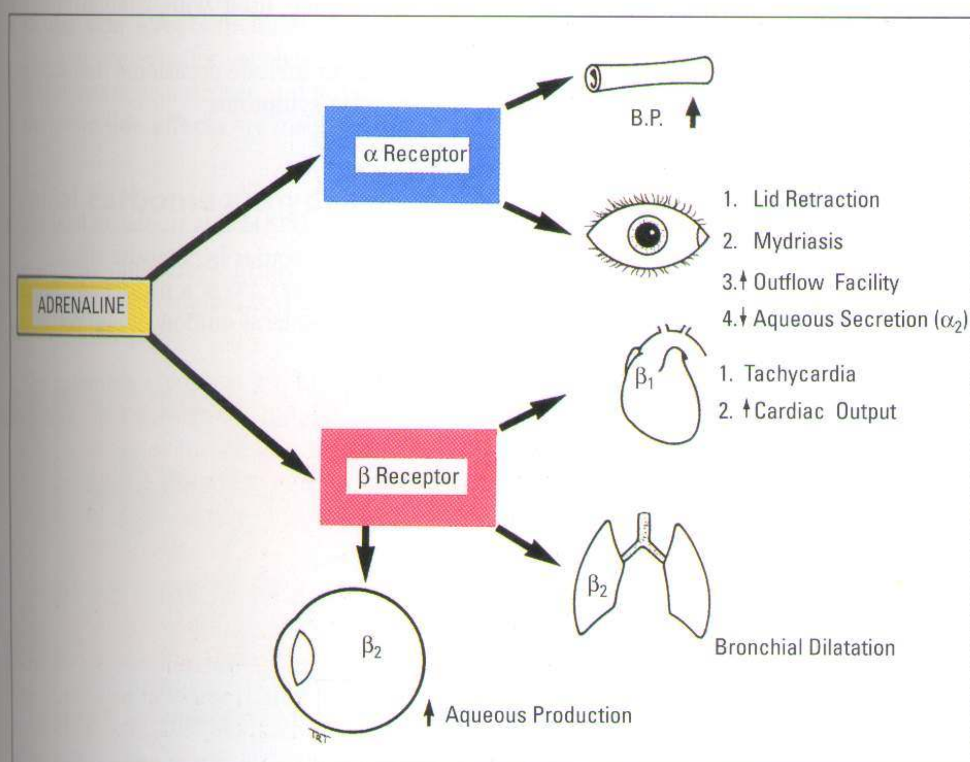


Fig. 9.139
Pharmacology of adrenergic neurones

minimized. Betaxolol is the only cardioselective agent currently available for the treatment of glaucoma. Contraindications to beta-blockers include congestive cardiac failure, second or third degree heart block, bradycardia, asthma and obstructive airways disease.

Timolol

1. **Preparations**
   - Timoptol 0.25%, 0.5% b.d.
   - Timoptol-LA 0.25%, 0.5% once daily.
   - Nyogel-LA 0.1% once daily.
2. **Ocular side effects** include occasional allergy, corneal punctate epithelial erosions and reduced aqueous tear secretion.
3. **Systemic side effects** tend to occur during the first week of administration. Although uncommon they may be serious.
   - Bradycardia and hypotension can result from beta-1 blockade. Beta-blockers are therefore contraindicated in patients with bradycardia and congestive cardiac failure.

> ***NB:*** The patient's pulse must be palpated before prescribing a beta-blocker.

   - Bronchospasm may be induced by beta-2 blockade and may be fatal in pre-existing asthma or severe chronic pulmonary obstruction.
   - Miscellaneous side effects include sleep disorders, hallucinations, confusion, depression, fatigue, headache, nausea, dizziness, decreased libido and possible reduction of plasma high-density lipoprotein level.
4. **Reduction of systemic drug absorption** may be achieved by:
   - Lacrimal occlusion following instillation, by closing the eyes and applying digital pressure over the lacrimal sac area for about 3 minutes. Apart from obstructing lacrimal drainage and reducing systemic absorption, this also prolongs eye–drug contact and increases therapeutic efficacy.
   - Merely closing the eyes for 3 minutes will reduce systemic absorption by about 50%.

Other beta-blockers

1. **Betaxolol** (Betoptic) 0.5% b.d. Although the ocular hypotensive effect is less than timolol, the effect on preservation of the visual field appears to be superior. Betaxolol may increase retinal blood flow by increasing perfusion pressure.
2. **Levobunolol** (Betagan) 0.5% is as potent as timolol. Once-daily administration is often adequate.
3. **Carteolol** (Teoptic) 1%, 2% is similar to timolol but also exhibits intrinsic sympathomimetic activity. It has a more selective action on the eye than on the cardiopulmonary system and may therefore induce less bradycardia than timolol.
4. **Metipranolol** 0.1%, 0.3% b.d. is similar to timolol, but is available only in preservative-free units. It is therefore useful in patients allergic to preservatives or wearing soft contact lenses (in whom benzalkonium chloride should be avoided). It may rarely cause anterior uveitis.

Alpha-2 agonists

These agents decrease IOP by both decreasing aqueous secretion and enhancing uveoscleral outflow.

1. **Brimonidine** (Alphagan) 0.2% b.d. is a highly selective alpha-2 agonist which also has a neuroprotective effect. Its efficacy is less than timolol but better than betaxolol. It exhibits additivity with beta-blockers. Its main ocular side effect is allergic conjunctivitis that may be delayed for up to a year after commencement of therapy. Systemic side effects include xerostomia, drowsiness and fatigue.
2. **Apraclonidine** (Iopidine) 0.5%, 1% is mainly used after laser surgery on the anterior segment to offset an acute rise in IOP. It is not suitable for long-term use because of tachyphylaxis (loss of therapeutic effect over time) and a high incidence of local side effects.

Prostaglandin analogues

Prostaglandin analogues reduce IOP by enhancing uveoscleral outflow.

Latanoprost

This is a prostaglandin F2-alpha analogue.

1. **Preparations**. Latanoprost (Xalatan) 0.005% used once daily.
2. **Efficacy** is superior to timolol although a proportion of patients show no response.
3. **Ocular side effects** include conjunctival hyperaemia, eyelash lengthening and hyperpigmentation of lashes, iris (Fig. 9.140) and periorbital skin. Anterior uveitis and cystoid macular oedema may rarely occur in predisposed eyes. The drug should therefore be used with caution in uveitic glaucoma.
4. **Systemic side effects** include occasional headache and upper respiratory tract symptoms.

Other preparations

1. **Travoprost** (Travatan) 0.004% is similar to latanoprost but may have a superior ocular hypotensive effect.
2. **Bimatoprost** (Lumigan) 0.3% is a prostamide. In addition to facilitating uveoscleral outflow, it also potentiates trabecular outflow.



Fig. 9.140
Right iris hyperchromia and hyperpigmentation of lashes due to latanoprost

3. **Unoprostone isopropyl** (Rescula) 0.15% b.d. is not as effective as latanoprost in lowering IOP and is perhaps unsuited for monotherapy. However, it may be used in combination with latanoprost.

Miotics

Mode of action

Miotics are parasympathomimetic drugs that act by stimulating muscarinic receptors in the sphincter pupillae and ciliary body.

1. **In primary open-angle glaucoma** miotics reduce IOP by contraction of the ciliary muscle, which increases the facility of aqueous outflow through the trabecular meshwork.
2. **In primary angle-closure glaucoma** contraction of the sphincter pupillae and the resultant miosis pulls the peripheral iris away from the trabeculum, thus opening the angle. It is often necessary to reduce IOP with systemic medication before miotics can take effect.

Pilocarpine

1. **Preparations**
   - Pilocarpine 1%, 2%, 3%, 4% is used q.i.d. as monotherapy. When used in combination with a beta-blocker, b.d. administration is adequate.
   - Pilocarpine gel (Pilogel) consists of pilocarpine adsorbed on to a plastic gel, instilled once daily at bedtime so that the induced myopia and miosis last only during sleep. The main disadvantage is the development of a diffuse superficial corneal haze in 20% of users, although this rarely affects visual acuity.
2. **Efficacy** is equal to beta-blockers.
3. **Ocular side effects** include miosis, brow ache, myopic shift and exacerbation of symptoms of cataract. Visual field defects appear denser and larger.
4. **Systemic side effects** are insignificant.

Topical carbonic anhydrase inhibitors

The carbonic anhydrase inhibitors (CAIs) are chemically related to the sulphonamides. They lower IOP by inhibiting aqueous secretion.

1. **Dorzolamide** (Trusopt) 2% t.i.d. is similar in efficacy to betaxolol but inferior to timolol. The main ocular side effect is allergic conjunctivitis.
2. **Brinzolamide** (Azopt) 1% t.i.d. is similar to dorzolamide, but with a lower incidence of local allergy.

Combined topical preparations

Combined preparations with similar ocular hypotensive effects to the sum of the individual components improve convenience and patient compliance. They are also more cost effective. Examples include:

1. **Cosopt** (timolol + dorzolamide) b.d.
2. **Xalacom** (timolol + latanoprost) once daily.
3. **TimPilo** (timolol + pilocarpine) b.d.

Systemic carbonic anhydrase inhibitors

Systemically administered CAIs are useful as short-term treatment; their long-term use is usually reserved for patients at high risk of visual loss.

Preparations

1. **Acetazolamide tablets** 250 mg. The dose is 250–1000 mg in divided doses. The onset of action is within 1 hour, with a peak at 4 hours and a duration up to 12 hours.
2. **Acetazolamide sustained-release capsules** 250 mg. The dose is 250–500 mg daily with a duration of up to 24 hours.
3. **Acetazolamide powder** 500 mg vials for injection. The onset of action is almost immediate, with a peak at 30 minutes and a duration of up to 4 hours. This is the only CAI preparation available for injection and is useful in acute angle-closure glaucoma.
4. **Dichlorphenamide tablets** 50 mg. The dose is 50–100 mg (2–3 times daily). The onset of action is within 1 hour, with a peak at 3 hours and a duration of up to 12 hours.
5. **Methazolamide tablets** 50 mg. The dose is 50–100 mg (2–3 times daily). The onset of action is within 3 hours, with a peak at 6 hours and a duration of up to 10–18 hours. This is a useful alternative to acetazolamide with a longer duration of action but is currently not available in the United Kingdom.

Systemic side effects

Long-term use of systemic CAIs is frequently limited by systemic side effects (Fig. 9.141). The patient should always be warned of potential side effects as this decreases anxiety and improves compliance.

1. **Common**
   a. *Paraesthesiae* characterized by tingling of the fingers, toes, hands or feet, and occasionally at the mucocutaneous junctions, is a universal finding and usually innocuous. Compliance is suspect if the patient denies this symptom.
   b. *The malaise complex* is characterized by a combination of malaise, fatigue, depression, weight loss and decreased libido. A supplemental 2-week course of sodium acetate may often be helpful.
2. **Uncommon**
   a. *The gastrointestinal complex* is characterized by gastric irritation, abdominal cramps, diarrhoea and nausea. This can occur independently of the malaise syndrome and is unrelated to any specific changes in blood chemistry.
   b. *Renal stone formation.*
   c. *Stevens–Johnson syndrome* may occur since CAIs are sulphonamide derivatives.

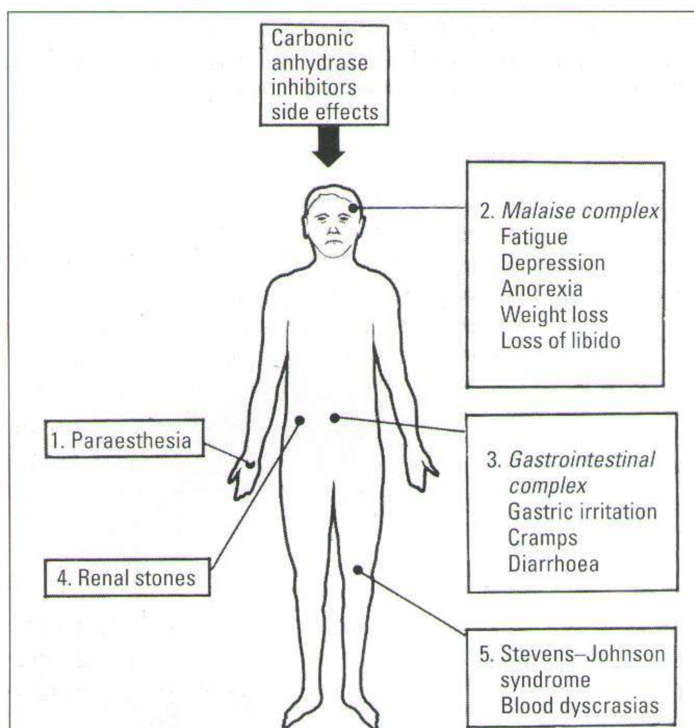


Fig. 9.141
Side effects of systemic carbonic anhydrase inhibitors

d. Blood dyscrasias are extremely rare and of two types:
- Dose-related bone marrow suppression which usually recovers when treatment is stopped.
- Idiosyncratic aplastic anaemia is not dose-related and has a mortality of 50%. It may occur after only one dose but usually does so during the first 2–3 months and very rarely after 6 months administration.

Hyperosmotic agents

Physiological principles

Osmotic pressure is dependent on the number rather than on the size of solute particles in a solution. Lower molecular weight solutes therefore exert a greater osmotic effect per gram. Hyperosmotic agents remain intravascular, thus increasing blood osmolality. They lower IOP by creating an osmotic gradient between blood and vitreous so that water is 'drawn out' from the vitreous. The higher this gradient the greater the reduction of IOP. To be effective in the eye, a hyperosmotic agent must therefore be unable to penetrate the blood–aqueous barrier. If penetration occurs, an osmotic equilibrium is set up and any further effect is lost. Hyperosmotic agents are therefore of limited value in the treatment of inflammatory glaucomas in which the integrity of the blood–aqueous barrier is compromised.

Clinical uses

When a temporary drop in IOP is required that cannot be obtained by other means.

- In acute angle-closure glaucoma .
- Prior to intraocular surgery when the IOP is very high, as may occur from dislocation of the lens into the anterior chamber.

> ***NB:*** These preparations should be given fairly rapidly and the patient should not subsequently be given fluids to quench thirst.

Preparations

1. **Glycerol** is an oral agent with a sweet and sickly taste. Pure lemon (not orange) juice often needs to be added to avoid nausea. The dose is 1 g/kg body weight or 2 ml/kg body weight (50% solution). Peak action is within 1 hour, with a duration up to 3 hours. Although glycerol is metabolized to glucose, it may be given to well-controlled diabetics.
2. **Isosorbide** is an oral agent with a minty taste. Metabolically inert, it may be given to diabetics without insulin cover. The dose is the same as for glycerol.
3. **Mannitol** is the most widely used intravenous hyperosmotic agent. The dose is 1 g/kg body weight or 5 ml/kg body weight (20% solution in water). Peak action is achieved within 30 minutes, with a duration of up to 6 hours.

Side effects

1. **Cardiovascular overload** may occur as a result of increased extracellular volume. Hyperosmotic agents should therefore be used with great caution in patients with cardiac or renal disease.
2. **Urinary retention** may occur in elderly men following intravenous administration. Catheterization may be necessary in those with prostatism.
3. **Miscellaneous** side effects include headache, backache, nausea and mental confusion.

Laser therapy

Argon laser trabeculoplasty

Argon laser trabeculoplasty (ALT) involves the application of discrete laser burns to the trabeculum. This enhances aqueous outflow and lowers IOP.

Technique

1. A drop of apraclonidine 1% or brimonidine 0.2% is instilled to prevent an early post-laser rise in IOP.
2. Two drops of a topical anaesthetic are instilled.
3. A goniolens is inserted with the mirror at the 12 o'clock position to visualize the inferior angle (usually the easiest part to see).
4. The scleral spur, Schwalbe line (which may be pigmented) and the three-dimensional ground-glass appearance of the trabeculum are identified.

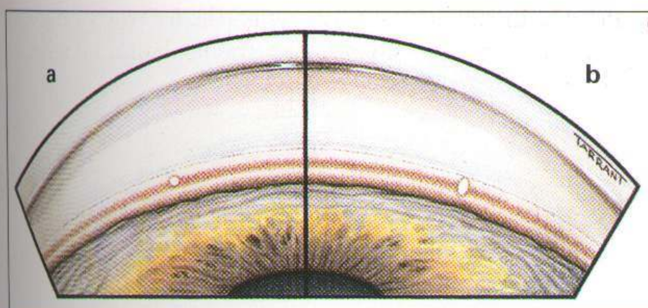


Fig. 9.142
Laser trabeculoplasty. (**a**) Correct round aiming beam; (**b**) incorrect oval aiming beam

5. The aiming beam is focused at the junction of the pigmented and non-pigmented trabeculum, ensuring that the spot is round and has a clear edge (Fig. 9.142a). An oval spot with a blurred outline (Fig. 9.142b) means that the aiming beam is not perpendicular to the trabecular surface.
6. Initial laser settings are commonly 50 μm spot size, 0.1 seconds duration and 700 mW power.
7. The laser is fired; the ideal reaction is a transient blanching (Fig. 9.143a) or the appearance of a minute gas bubble (Fig. 9.143b) at the point of incidence. A large gas bubble (Fig. 9.143c) is excessive.
8. If the reaction is inadequate, the power is increased by 200 mW steps. In heavily pigmented angles, a power setting of 400 mW may suffice, whereas a non-pigmented meshwork may require up to 1200 mW (the average is about 900 mW).
9. Twenty-five burns are applied at regularly spaced intervals from one end of the mirror to the other.
10. The goniolens is rotated clockwise by 90° and a further 25 burns applied, making a total of 50 over 180° of the angle. It is important to be familiar with the rotational pattern of the mirror so that adjacent quadrants are treated systematically. With practice it is possible to perform ALT by continuously rotating the goniolens and applying each burn through the centre of the mirror.

> *NB:* Some ophthalmologists initially treat 180° and later treat the other 180° if the response is unsatisfactory. Others, however, treat the entire circumference with 100 burns at the initial sitting.

11. Iopidine 1% or brimonidine 0.2% is instilled.
12. Topical fluorometholone q.i.d. for a week is prescribed; glaucoma medical therapy is continued.

Follow-up

Four to six weeks should be allowed for the treatment to take effect. If the IOP is reduced significantly by 6 weeks, gradual withdrawal of medication may be attempted, although total withdrawal is seldom possible. The main aim of ALT is to obtain a safe IOP; the reduction of medication is usually a secondary consideration. If IOP remains high and only 180° have been treated, the remaining 180° are treated. Following 360° ALT, re-treatment is unlikely to be beneficial and filtration surgery merits consideration.

Complications

1. **Peripheral anterior synechiae** (Fig. 9.143d) may develop if the burns are applied too posteriorly or if the energy level is high. In the majority of cases this does not compromise aqueous outflow.
2. **Small haemorrhages** may develop if the blood vessels on the peripheral iris or ciliary body are inadvertently treated. Such bleeding is easily stopped by applying pressure on the globe with the goniolens.
3. **Acute elevation of IOP** may occur if prophylactic apraclonidine or brimonidine is not used.
4. **Anterior uveitis** is fairly common but usually mild, transient and innocuous.
5. **Adverse effect on subsequent filtration surgery**. The incidence of encapsulated blebs following filtration surgery is up to three times higher in eyes previously treated with ALT.

Results

1. **In POAG** the initial success rate is 75–85%. The average reduction of IOP is about 30%; eyes with initially high IOPs therefore manifest a greater reduction of IOP. Up to 50% of eyes are still controlled after 5 years and about 33% after 10 years. Failure occurs most frequently in the first year; therefore if the IOP is still controlled at 1 year, the probability of control after 5 years is 65% and after 10 years about 40%. If ALT is used as primary treatment,

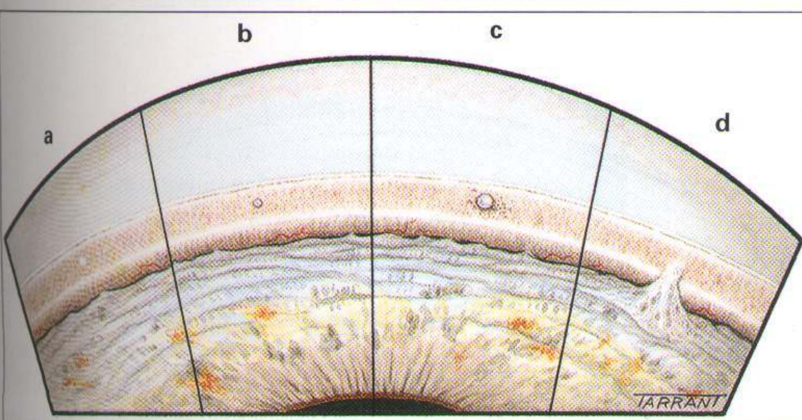


Fig. 9.143
Laser trabeculoplasty. (**a**) Blanching of the trabeculum: correct reaction; (**b**) small bubble: also correct reaction; (**c**) large bubble: excessive reaction; (**d**) peripheral anterior synechiae: burn applied too posteriorly

50% of cases require additional medical therapy within 2 years. Following initially successful ALT, re-treatment carries a low success rate (30% after 1 year and only 15% after 2 years). In general, the results are less good in patients under the age of 50 years. Black patients respond as well as white initially, but tend to have a more rapid loss of effect.

2. **In normal-tension glaucoma** 50–70% of patients have a good response, but the absolute reduction in IOP is less than in POAG.
3. **In pigmentary glaucoma** results are generally good, though less so in older patients.
4. **In pseudoexfoliation glaucoma** initial results are excellent, although failure may occur earlier than in POAG and subsequent rise in IOP may be rapid.

> *NB:* ALT is ineffective in paediatric and most secondary glaucomas with the exception of pigmentary and pseudo-exfoliation glaucoma.

Diode laser trabeculoplasty

This gives similar results to ALT, although with less disruption of the blood–aqueous barrier. The following are the main practical differences between the two modalities:

- A higher laser power of 800–1200 mW is used.
- The burns are less intense; although blanching is observed bubble formation does not occur.
- The spot size is 100 μm but can be reduced to 70 μm by using a special contact lens.
- The pulse duration is 0.1 or 0.2 seconds.

Nd:YAG laser iridotomy

Indications

- Primary angle-closure glaucoma: acute, intermittent and chronic.
- Fellow eye of a patient with acute glaucoma.
- Narrow 'occludable' angles.
- Secondary angle closure with pupil block.
- POAG with narrow angles and combined mechanism glaucoma.

Technique

1. A drop of apraclonidine 1% or brimonidine 0.2% is instilled.
2. The pupil should ideally be miosed with topical pilocarpine, although this may not be possible following acute glaucoma.
3. A topical anaesthetic is instilled.
4. A special contact lens such as the Abraham iridotomy lens is inserted (Fig. 9.144).
5. A site is selected, preferably in the superior iris, so that it is covered by the eyelid thus preventing monocular diplopia. The iridotomy should also be as peripheral as possible to minimize damage to the crystalline lens, although an arcus senilis may render this difficult. Finding an iris crypt is beneficial but not essential.



Fig. 9.144
Abraham lens used for laser iridotomy

6. The beam is angled so that it is non-perpendicular and aimed towards the peripheral retina to avoid the remote possibility of a macular burn.
7. *Laser settings vary with different machines.* Most iridotomies are made with settings of 4–8 millijoules (mJ). For a thin blue iris the required energy level is 1–4 mJ per shot, with two to three shots per burst. Thick velvety smooth, brown irides necessitate higher energy levels, which may be achieved with higher power or more shots per burst. Although such higher energy levels and more shots per burst render penetration of the iris easier, they carry an increased risk of intraocular damage.

> *NB:* As a general guideline three bursts of 3–6 mJ are usually effective.

8. The beam is focused precisely and the laser fired. Successful penetration is characterized by a gush of pigment debris. On average seven shots are required to produce an adequate iridotomy (Fig. 9.145) although with practice this can be reduced to one or two.
9. A drop of apraclonidine 1% or brimonidine 0.2% is instilled.
10. A strong topical steroid is prescribed every 10 minutes for 30 minutes and then hourly on the day of treatment and then q.i.d. for 1 week.

Potential technical problems

1. **Initial failure** is managed by re-treating the same site or moving to a different site and increasing the energy level. The decision to re-treat the same site depends in part on the degree of pigment dispersion and haemorrhage caused by the previous partial treatment. In thick brown irides, incomplete treatment may result in a *thick cloud of* dispersed iris pigment which impairs visualization and accurate focusing on the base of the crater. Further applications applied into the cloud often merely increase

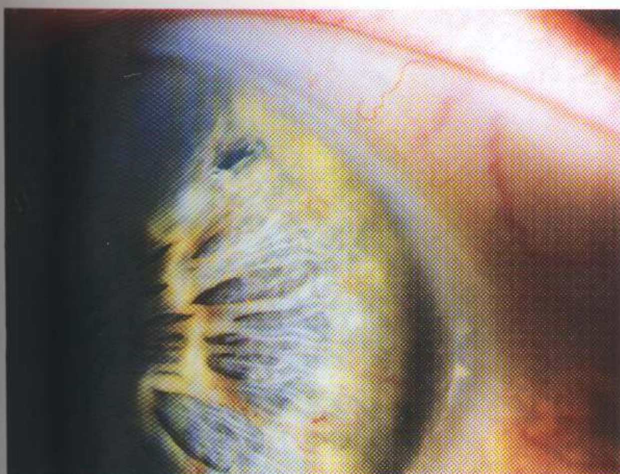


Fig. 9.145
Correct size opening in the iris

the pigment and haemorrhage, without producing an opening. In this situation it is best to wait for the cloud to disperse and then re-treat the same site, or to increase the energy level and try a different site. Alternatively a potential site may be pre-treated with an argon laser.

2. **Opening too small**. It is sometimes easier to create an additional opening at a different site rather than to try to enlarge the opening. The ideal diameter is 150–200 μm.

Complications

1. **Bleeding** occurs in about 50% of cases. It is usually slight and stops after several seconds. Persistent bleeding can be terminated by pressing the contact lens against the cornea.
2. **Iritis** is common and usually mild. Severe iritis, which may result in the formation of posterior synechiae (Fig. 9.146), is invariably caused by over-treatment and inadequate post-laser steroid therapy.
3. **Corneal burns** may occur if a contact lens is not used or if the anterior chamber is shallow.
4. **Glare and diplopia** may rarely occur if the iridotomy is not sited under the upper eyelid.

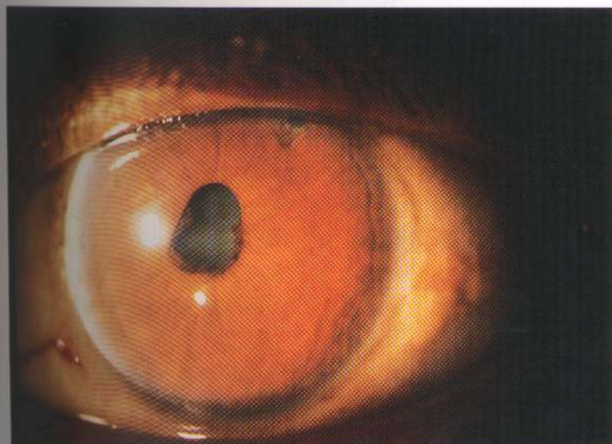


Fig. 9.146
Posterior synechiae following laser iridotomy (Courtesy of J. Salmon)

Diode laser cycloablation

This procedure lowers IOP by destroying part of the secretory ciliary epithelium, thereby reducing aqueous secretion. It is used mainly to control pain in intractable end-stage glaucoma, usually associated with permanent synechial angle closure.

1. **Technique**
   a. A peribulbar or sub-Tenon anaesthetic is administered.
   b. Laser settings are 1.5 seconds and 1500–2000 mW.
   c. The power is adjusted until a 'popping' sound is heard and then reduced to just below that level.
   d. Approximately 30 burns are placed 1.4 mm posteriorly to the limbus over 270°.
   e. A strong topical steroid is prescribed hourly on the day of treatment and then q.i.d. for 2 weeks.
2. **Complications**. Mild pain and anterior segment inflammation are common. Serious complications are rare and include chronic hypotony, scleral thinning, corneal decompensation and retinal or choroidal detachment. However, since the aim of the procedure is usually to relieve pain, vision-threatening complications do not have the same significance as those following conventional filtering procedures.
3. **Results**. The success rate is dependent on the type of glaucoma; frequently the procedure has to be repeated. Pain relief is generally good, but does not appear to be solely related to pressure control.

Trabeculectomy

Surgical techniques

Trabeculectomy

A trabeculectomy is a surgical procedure that lowers IOP by creating a fistula, which allows aqueous outflow from the anterior chamber to the sub-Tenon space. The fistula is protected or 'guarded' by a superficial scleral flap (Fig. 9.147).

1. The pupil must be miosed.
2. A flap of conjunctiva and Tenon capsule is fashioned. The flap may be limbal or fornix-based (Fig. 9.148).
3. Episcleral tissue is cleared. An outline of the proposed superficial scleral flap is made with wet-field cautery.
4. Incisions are made along the cautery marks through two-thirds of scleral thickness, to create a 'trapdoor' lamellar scleral flap (Fig. 9.149). This flap may be rectangular (3 × 4 mm) or triangular, according to preference.
5. The superficial flap is dissected forwards until clear cornea has been reached (Fig. 9.150).
6. A paracentesis is made in superotemporal peripheral clear cornea.
7. The anterior chamber is entered along the entire width of the trapdoor flap.

8. A block of deep sclera (1.5 × 2 mm) is excised with a knife and scissors (Figs 9.151 and 9.152) or a special punch (Fig. 9.153).
9. A peripheral iridectomy is performed (Fig. 9.154) in order to prevent blockage of the internal opening by the peripheral iris. Figure 9.155 shows the appearance from inside the eye.
10. The superficial scleral flap is sutured at its posterior corners so that it is lightly apposed to the underlying bed.
11. Alternatively, the flap may be sutured tightly with releasable sutures to reduce the risk of postoperative scleral flap leakage and shallow anterior chamber.
12. Balanced salt solution is injected into the anterior chamber through the paracentesis (Fig. 9.156a). This tests the patency of the fistula and facilitates the detection of any holes or leaks in the flap.

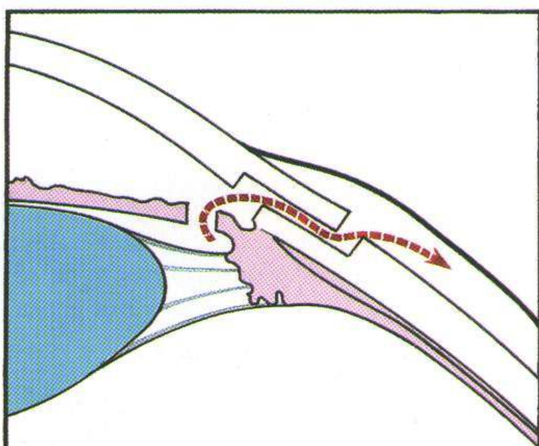


Fig. 9.147
Pathway of aqueous egress following trabeculectomy

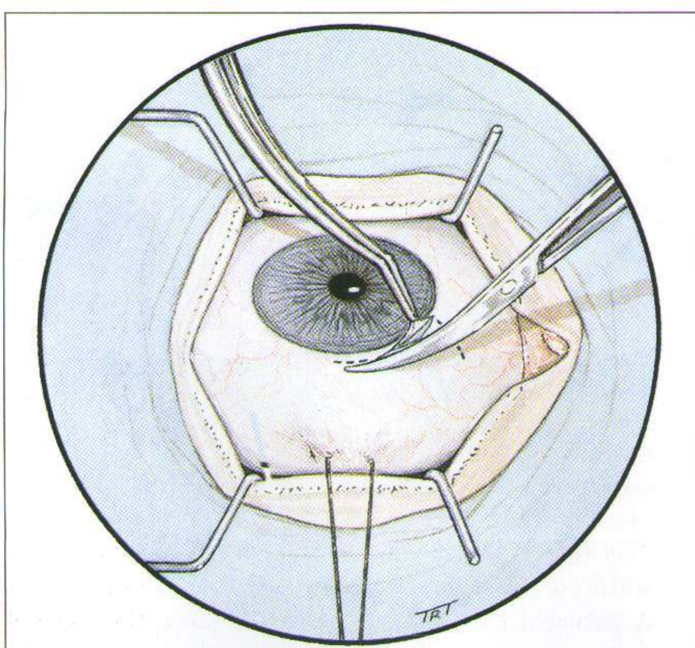


Fig. 9.148
Limbal conjunctival incision for a fornix-based flap

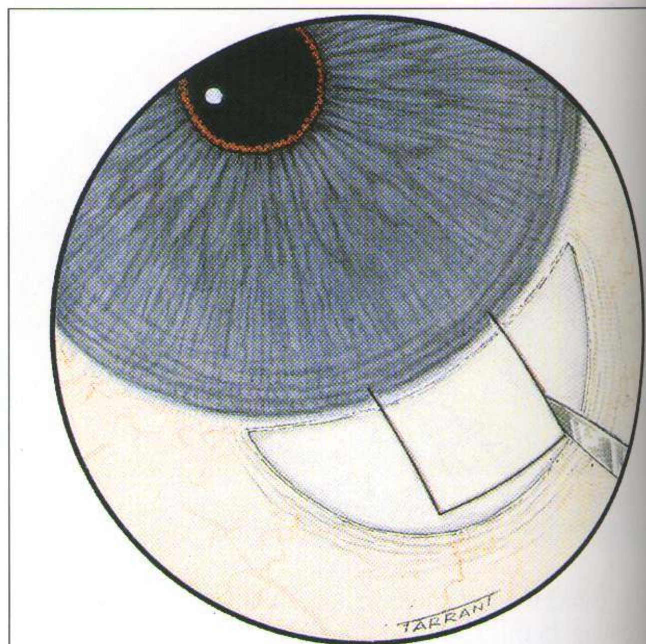


Fig. 9.149
Outline of the superficial scleral flap

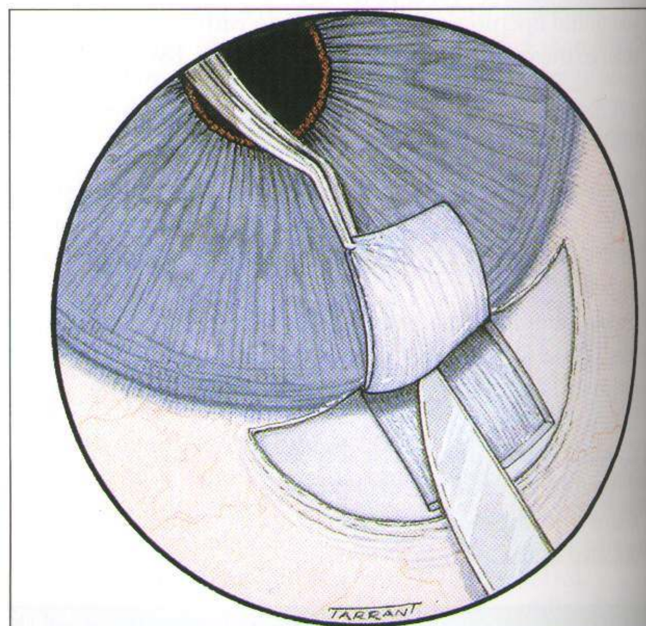


Fig. 9.150
Dissection of the superficial scleral flap

13. Conjunctiva/Tenon capsule flap is sutured (Fig. 9.156b). Irrigation through the paracentesis is repeated to produce a bleb, which is then checked for leakage.
14. A drop of atropine 1% is instilled.
15. A steroid and an antibiotic are injected under the inferior conjunctiva.

Combined trabeculectomy and phacoemulsification

Trabeculectomy and phacoemulsification can be performed using the same conjunctival and scleral incisions as follows:

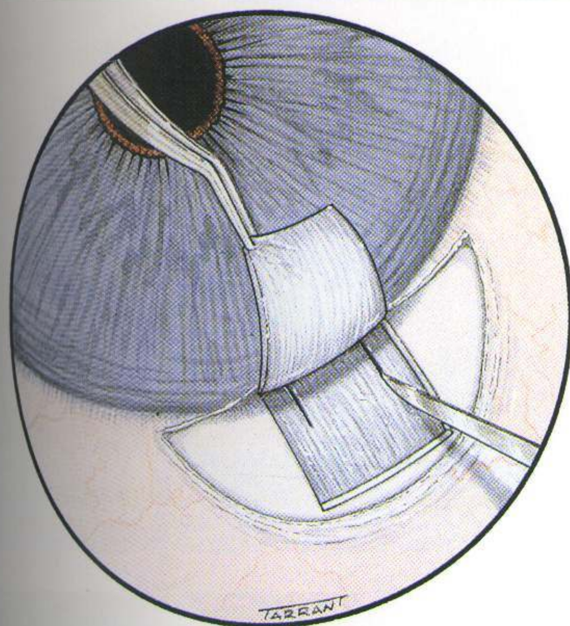


Fig. 9.151
Incisions for the deep sclerectomy

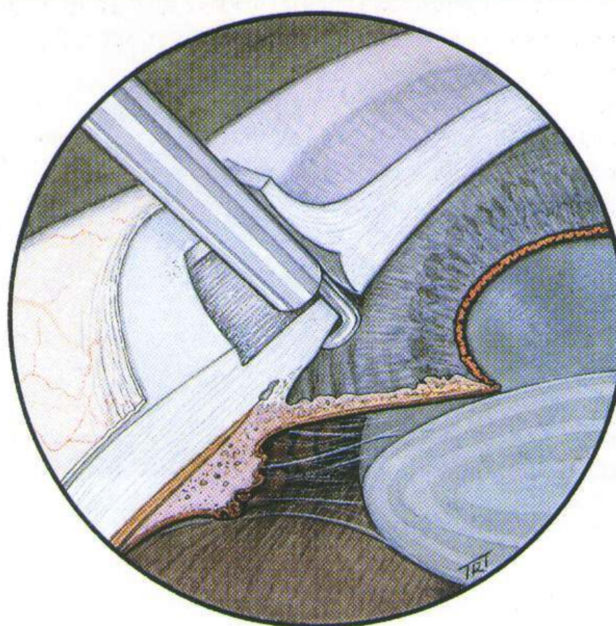


Fig. 9.153
Excision of the deep block with a punch

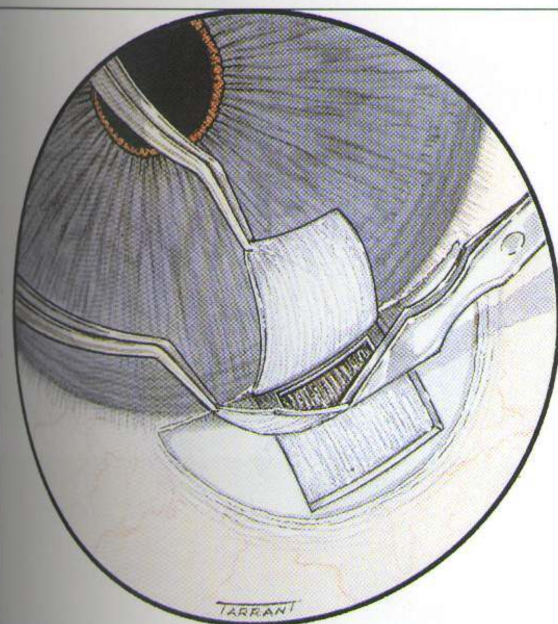


Fig. 9.152
Excision of the deep block with Vannas scissors

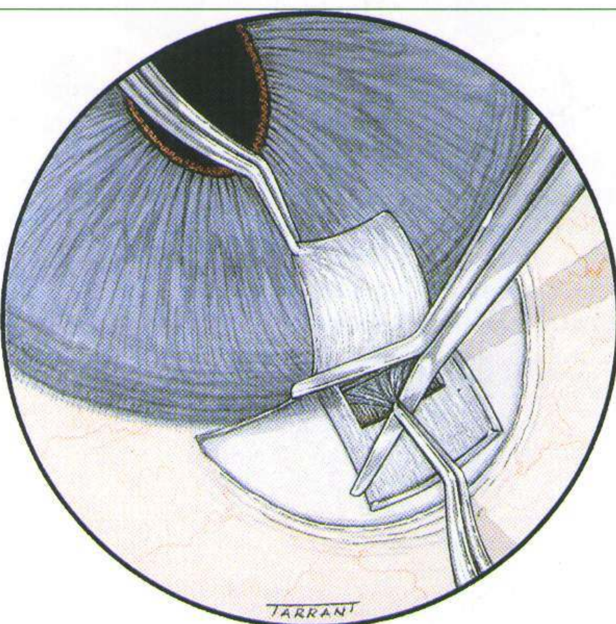


Fig. 9.154
Peripheral iridectomy

1. A conjunctival flap is fashioned.
2. A lamellar scleral flap 3.5–4 mm wide, hinged at the limbus, is dissected.
3. A 'phaco' incision 2.8–3.2 mm wide is made into the anterior chamber.
4. Phacoemulsification is performed in the usual manner.
5. A foldable intraocular lens is inserted. If a rigid lens is used, the dimensions of the conjunctival and scleral flaps are adjusted accordingly from the outset.
6. The deep scleral block is removed.
7. A peripheral iridectomy is performed.
8. The scleral flap is closed.
9. Tenon capsule and conjunctiva are sutured.

Postoperative complications

Shallow anterior chamber

This is one of the most common complications after trabeculectomy, and may be due to (a) *pupillary block*, (b) *overfiltration* or (c) *malignant glaucoma* (aqueous misdirection). Severe and sustained shallowing is uncommon, the chamber re-forming spontaneously in most cases. However, those that do not may develop severe complications such as peripheral anterior synechiae, corneal endothelial damage, cataract and hypotony-associated maculopathy.

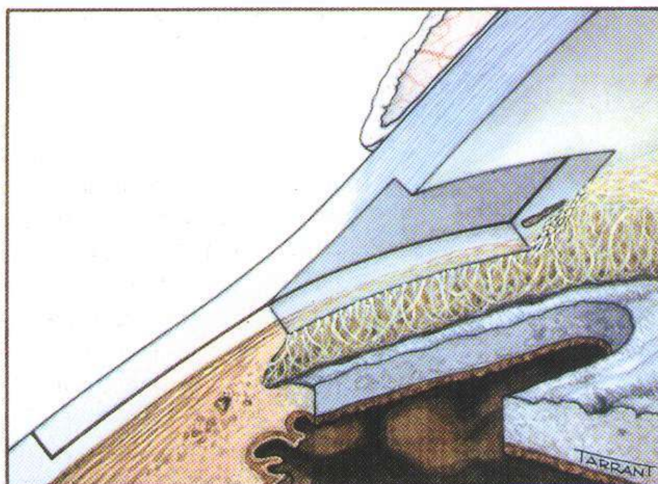


Fig. 9.155
Appearance following completed trabeculectomy

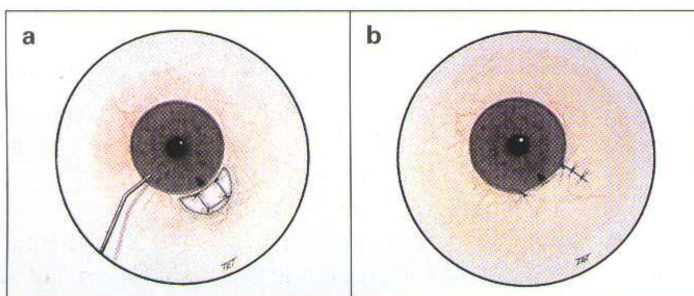


Fig. 9.156
(**a**) Injection of balanced salt solution into the anterior chamber; (**b**) sutured fornix-based flap



Fig. 9.157
Shallow anterior chamber with peripheral iridocorneal apposition

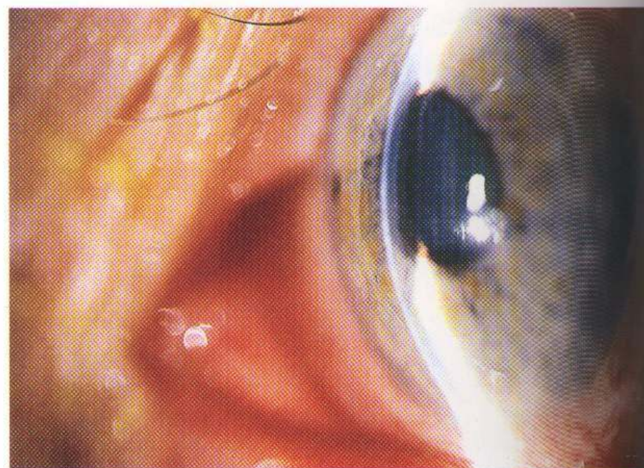


Fig. 9.158
Very shallow anterior chamber with pupillary border–corneal apposition

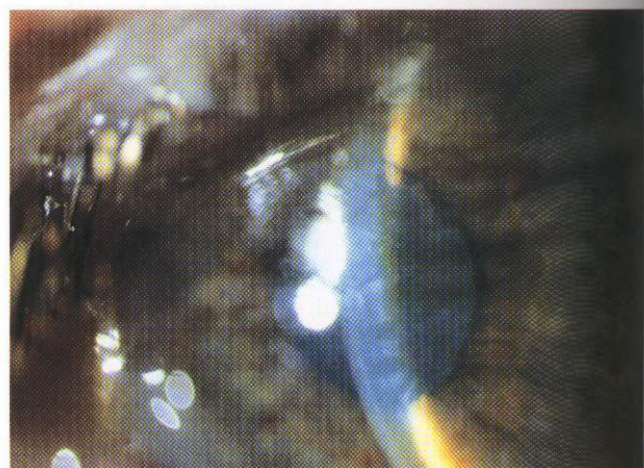


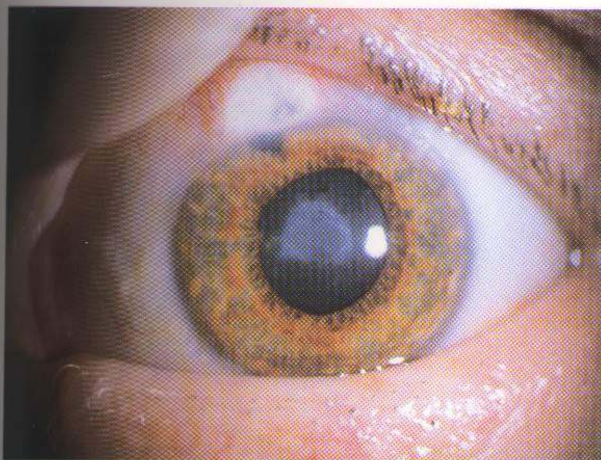
Fig. 9.159
Lenticulo-corneal touch resulting in corneal oedema

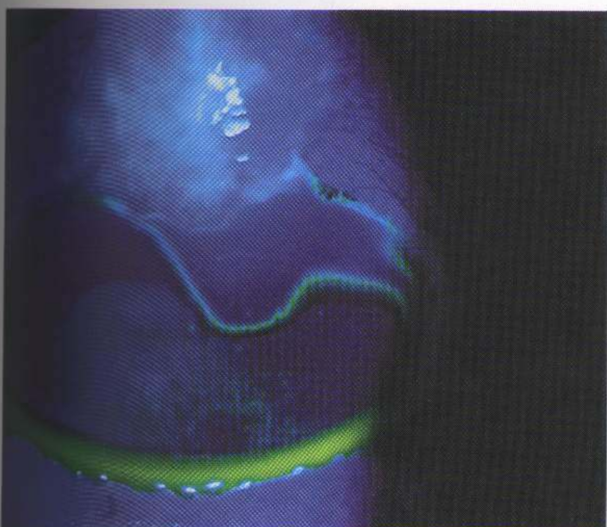
Evaluation

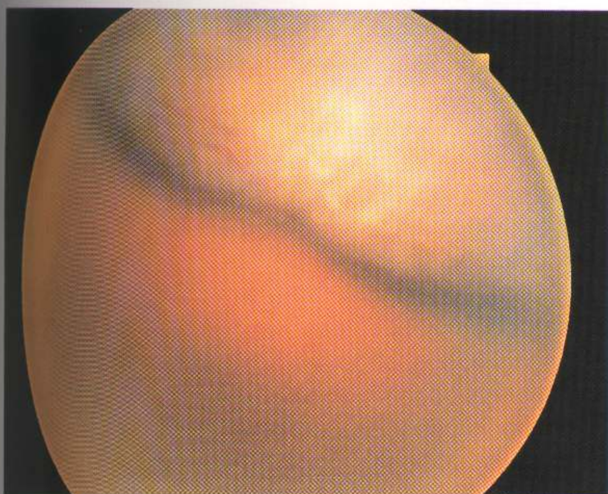
1. **Severity** of shallowing can be graded as follows:
   - Grade 1: peripheral iris apposition to the posterior corneal surface (Fig. 9.157).
   - Grade 2: pupillary border–corneal apposition (Fig. 9.158).
   - Grade 3: lens–corneal touch which, if unrelieved, may lead to endothelial decompensation (Fig. 9.159) and cataract formation (Fig. 9.160).
2. **The cause** is determined as follows:
   - The patency of the peripheral iridectomy is confirmed and the configuration of the iris studied to rule out pupillary block.
   - The filtration bleb is assessed.
   - A Seidel test is performed by instilling 2% fluorescein into the conjunctival sac or over the bleb. The bleb is then observed with a cobalt blue filter; if leaking, the fluorescein will become diluted by escaping aqueous (Fig. 9.161). Diluted fluorescein fluoresces bright green in contrast with 2% fluorescein (not as strongly).
   - The IOP is measured.
   - The fundus is examined for the presence of choroidal detachments (Fig. 9.162).

Pupillary block

1. **Cause** is a non-patent peripheral iridectomy.
2. **Signs**. High IOP, flat bleb, negative Seidel test and iris bombé with a non-patent iridectomy.
3. **Treatment**. Argon laser may be applied to the pigment epithelium at the iridectomy site if the anterior iris stroma


Fig. 9.160
Anterior lens opacities following inappropriate management of a flat anterior chamber


Fig. 9.161
Positive Seidel test


Fig. 9.162
Choroidal detachment associated with hypotony

appears to have been largely penetrated, or a new laser iridotomy is performed.

Overfiltration

1. Causes

a. ***Scleral flap leakage*** due to insufficient resistance to outflow by the lamellar scleral flap. This can be prevented by initial tight closure of the flap with the option of subsequently increasing outflow in the early postoperative period by disrupting the sutures with an argon laser or releasing sutures that have been tied with slipknots. These manoeuvres are ineffective if undertaken later than 14 days postoperatively.

b. ***Bleb leakage*** through an inadvertent buttonhole or due to inadequate closure of the conjunctiva and Tenon capsule is perhaps the most common cause.

2. Signs.

- Low IOP.
- The bleb is well formed in a scleral flap leak and flat in a bleb leak.
- The Seidel test is negative in a scleral flap leak and positive in a bleb leak.
- The cornea may manifest signs of hypotony such as folds in Descemet membrane.
- Choroidal detachment may be present.

3. Treatment depends on the cause and degree of shallowing.

a. ***Initial*** conservative treatment in eyes without lenticulo-corneal touch.

- Topical atropine 1% to keep the pupil well dilated and prevent pupil block.
- Aqueous suppression with topical beta-blockers or oral acetazolamide may promote spontaneous healing by temporarily reducing aqueous flow through the fistula.
- Pinpoint bleb leaks may be sealed with cyanoacrylate or fibrin glue but sizeable conjunctival buttonholes or leaky incisions should be repaired surgically.
- In most cases this approach will be successful and the chamber will re-form within a few days.

b. ***Subsequent*** treatment if the aforementioned measures are ineffective involves temporary tamponade of the conjunctiva to enhance spontaneous healing by simple pressure patching, a large-diameter soft bandage contact lens, a collagen shield or a Simmons shell designed for the purpose. Such tamponade may result in deepening of the anterior chamber within a few hours, but if ineffective should be discontinued.

c. ***Definitive*** treatment for progressive shallowing and imminent or established lenticulo-corneal touch:

- The anterior chamber is re-formed with air, sodium hyaluronate or gas (SF_6).
- Choroidal detachment is drained only if very deep and in danger of touching (kissing choroidals).
- The scleral flap and conjunctiva are re-sutured. This may be difficult, since the tissue may now be friable.

Malignant glaucoma

Malignant (ciliary-block) glaucoma (aqueous misdirection 'syndrome') is rare but serious.

1. **Cause**. Blockage of aqueous flow at the pars plicata of the ciliary body, so that the aqueous is forced backwards into the vitreous.
2. **Signs**. A shallow anterior chamber in association with high IOP, absent bleb and negative Seidel test.
3. **Treatment**
   *a. **Initial conservative*** treatment.
   - Topical mydriatics (atropine 1% and phenylephrine 10%) to dilate the ciliary ring. This increases the distance between the ciliary processes and the equator of the lens, thereby tightening the zonule and pulling the lens posteriorly into its normal position.
   - Intravenous mannitol may be used if mydriatics are ineffective in order to shrink the vitreous gel and allow the lens to move posteriorly.
   - Aqueous suppressants are useful as adjuncts to control pressure.

   *b. **Subsequent*** treatment if medical therapy fails:
   - Nd:YAG laser may be fired through the iridectomy in order to disrupt the anterior hyaloid face and break the ciliary block. In pseudophakic eyes posterior capsulotomy and disruption of the anterior hyaloid face should be performed.
   - Pars plana vitrectomy is performed if laser therapy fails. Sufficient vitreous gel is excised to allow free flow of aqueous to the anterior chamber. If a vitreous cutter is not available the entrapped fluid may be aspirated with a 20-gauge needle inserted 3.5 mm posterior to the limbus and directed towards the centre of the globe.

Failure of filtration

Clinical evaluation

1. **Good filtration** is characterized by a low IOP and a bleb, which may take one of the following appearances:
   *a. **Type 1*** has a thin and polycystic appearance (Fig. 9.163) often with transconjunctival flow of aqueous.



Fig. 9.163
Thin polycystic filtration bleb

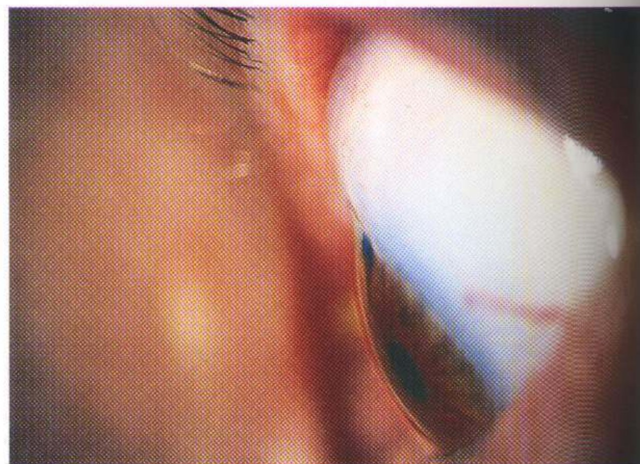


Fig. 9.164
Shallow diffuse filtration bleb

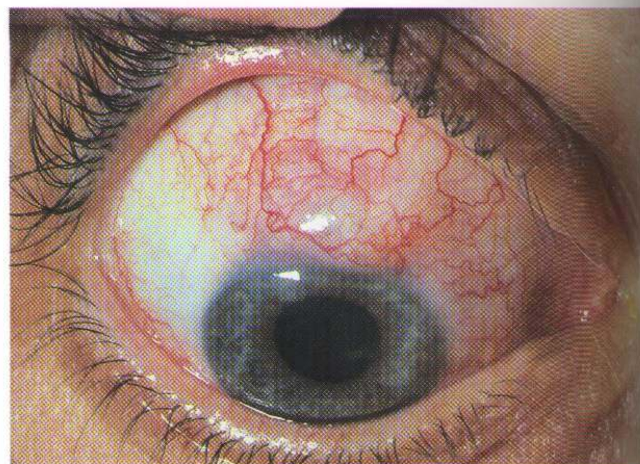


Fig. 9.165
Vascularized non-filtering bleb (Courtesy of J. Salmon)

   *b. **Type 2*** is shallow, thin-walled and diffuse, with a relatively avascular appearance in comparison with the surrounding conjunctiva (Fig. 9.164). Conjunctival epithelial microcysts are usually visible with high magnification.
2. **Poor filtration** is indicated by increasing IOP and a bleb with one of the following appearances:
   *a. **Type 3*** due to episcleral fibrosis, is flat, unassociated with microcystic spaces and manifests engorged surface blood vessels (Fig. 9.165).
   *b. **Type 4*** is an encapsulated bleb (Tenon cyst) which typically develops 2–8 weeks postoperatively. It is characterized by a localized, highly elevated, dome-shaped, firm, fluid-filled cavity of hypertrophied Tenon capsule with engorged surface blood vessels (Fig. 9.166). The cavity entraps aqueous humour and prevents filtration, although in some cases the IOP may not be elevated due to functional areas of filtration surrounding the bleb. Risk factors for encapsulated bleb formation include previous conjunctival surgery, laser trabeculoplasty, topical sympathomimetic therapy and an encapsulated bleb in the fellow eye.

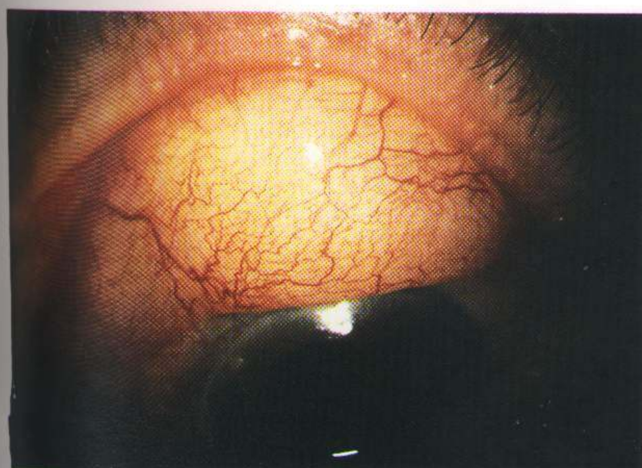


Fig. 9.166
Encapsulated non-filtering bleb

Causes of failure

These can be classified according to the site of blockage:

1. Extraocular
- Subconjunctival and episcleral fibrosis is the most common cause of bleb failure; in many cases a well-formed bleb is never established. Intra- or postoperative subconjunctival haemorrhage may increase the risk of subsequent fibrosis.
- Bleb encapsulation.

2. Scleral
- Over-tight suturing of the scleral flap.
- Gradual scarring in the scleral bed may lead to obstruction of the fistula at that level.

3. Intraocular
- Blockage of the sclerostomy by vitreous, blood or uveal tissue.
- Obstruction of the internal opening by a variety of thin membranes derived from surrounding cornea or sclera. This may be associated with poor surgical technique.

Management of failure

This is dependent on the aetiology and may involve one or more of the following:

1. **Ocular compression** in an effort to force outflow through the surgical fistula is performed as follows:
   a. *Digital compression* is performed through the lower lid with the eyes closed and the patient looking straight ahead. Moderate digital pressure is applied for 5–10 seconds; the bleb is then examined. If the fistula is completely occluded the IOP and bleb appearance will be unchanged. If compression is effective, the IOP will have fallen and the bleb often appears inflated. The patient is instructed to carefully repeat this manoeuvre several times a day.
   b. *Focal compression* under topical anaesthesia is applied at the slit-lamp with a moistened sterile cotton bud at the edge of the scleral flap in an attempt to promote outflow.
2. **Suture manipulation** may be considered 7–14 days postoperatively if the eye has high IOP, a flat bleb and a deep anterior chamber.
   a. *Releasable sutures* can be cut or released according to the technique of initial placement.
   b. *Argon laser suture lysis* is useful if releasable sutures have not been used. It may be performed through a Hoskins (suture lysis lens) or a Zeiss four-mirror goniolens. The laser settings are 0.2 seconds duration, 50 μm spot size and 500–700 mW power.
3. **Needling** of an encysted bleb may be performed at the slit-lamp or operating microscope under topical anaesthesia. Balanced salt solution is injected subconjunctivally adjacent to the encapsulated bleb through a 27-gauge needle on a 1 ml syringe. The needle is then used to transfix and create a 2 mm incision in the fibrous wall of the cyst, taking care not to buttonhole the conjunctiva.
4. **Subconjunctival injection of 5-fluorouracil** may be used in the first 7–14 days to suppress episcleral fibrosis; 5 mg (0.1 ml of 50 mg/ml solution) is injected approximately 10 mm away from the bleb.
5. **Nd:YAG laser** may be useful in two settings:
   a. *Internal* gonioscopic reopening of a blocked internal ostium provided the tissue responsible can be identified gonioscopically and the eye already has a well-established bleb.
   b. *External* transconjunctival revision of a late-failing bleb due to episcleral fibrosis.
6. **Reoperation** to revise the existing trabeculectomy or perform a second filtering procedure in a different location. In these cases, adjunctive antimetabolite therapy may be appropriate to increase the chances of a successful outcome.
7. **Medical therapy** may need to be resumed if all else fails.

Late bleb leakage

1. **The cause** is dissolution of conjunctiva overlying the sclerostomy, following previous operative application of antimetabolites, particularly mitomycin C. Necrosis of the

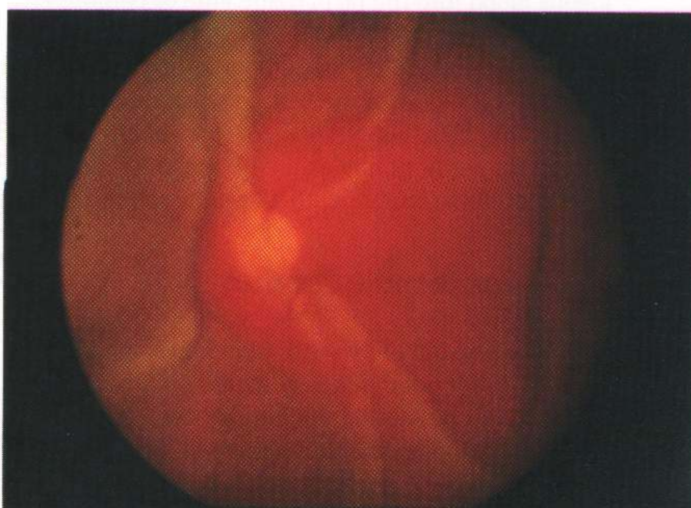
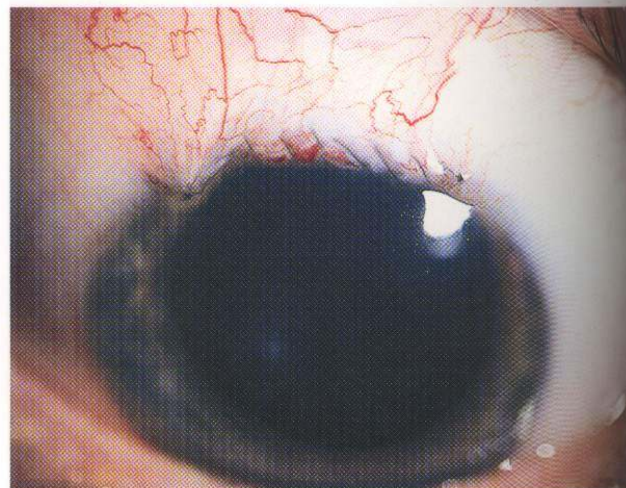


Fig. 9.167
Severe chorioretinal folds in a hypotonous eye


Fig. 9.168
Avascular cystic bleb


Fig. 9.169
Appearance following repair of a leaking bleb

surface epithelium results in transconjunctival drainage of aqueous.

2. **Complications** of untreated leaks include corneal decompensation, peripheral anterior synechiae, suprachoroidal haemorrhage, chorioretinal folds (Fig. 9.167), hypotonous maculopathy and infection.
3. **Signs**
   - Low IOP and an avascular cystic bleb (Fig. 9.168).
   - Seidel testing is initially negative, and only multiple punctate staining areas (sweating) are seen. Later frank hole formation results in gross leakage with a positive test.
   - Shallow anterior chamber and choroidal detachment may be present in severe cases.
4. **Treatment** is difficult. The following are some of the methods used, none of which are universally successful.
   a. ***Initial*** treatment is as for early postoperative overfiltration but is seldom successful.
   b. ***Subsequent*** treatment depends on whether the leakage involves merely 'sweating' or is due to hole formation:
      - Sweating blebs may be treated by injection of autologous blood into the bleb, tissue glue or compressive sutures.
      - Full-thickness holes usually require revisional surgery such as conjunctival advancement to hood the existing bleb (Fig. 9.169), free conjunctival patch autografts with removal of the existing bleb and scleral grafts to limit flow through the sclerostomy.

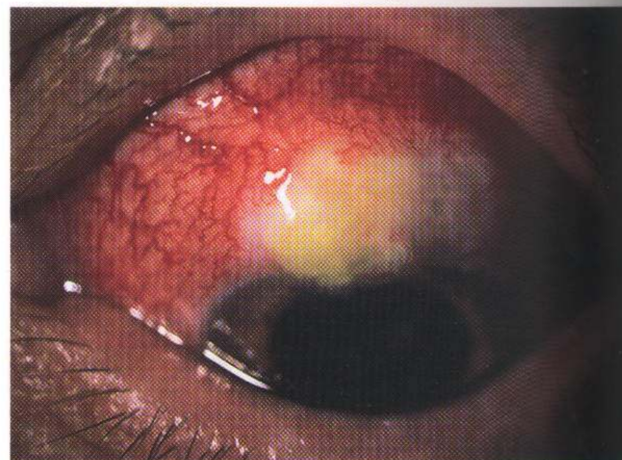
Late onset bacterial infection

The thin-walled cystic bleb with a positive Seidel test, particularly if associated with a history of adjunctive antimetabolite therapy, is at significant risk because it drains transconjunctivally and is, therefore, most likely to provide a pathway for the entry of bacteria into the eye. All patients with such blebs should be warned of the possibility of late infection and strongly advised to report immediately should they develop a red and sticky eye, or blurred vision. Procedures that may traumatize the bleb such as fitting of contact lenses or gonioscopy should be avoided if possible. Other risk factors include full-thickness drainage procedures (e.g. Scheie thermosclerostomy), inferior location of the filtering bleb and inappropriate intermittent or prolonged use of topical antibiotics after the postoperative period.

'Blebitis'

In 'blebitis' the infection does not involve the vitreous.

1. **Presentation** is with mild symptoms such as discomfort and redness, which have usually been present for several days.
2. **Signs**
   - A whitened, milky bleb that appears to contain inflammatory material (Fig. 9.170).
   - Anterior uveitis may be absent (stage 1 blebitis) or present (stage 2 blebitis).
   - The red reflex is normal.
3. **Treatment** involves topical fluoroquinolones similar to that for bacterial keratitis (*see* Chapter 5). This is usually adequate but the patient should be watched carefully for evidence of vitreous involvement which may occasionally occur.


Fig. 9.170
'Blebitis' following trabeculectomy characterized by a white drainage bleb with surrounding conjunctival injection

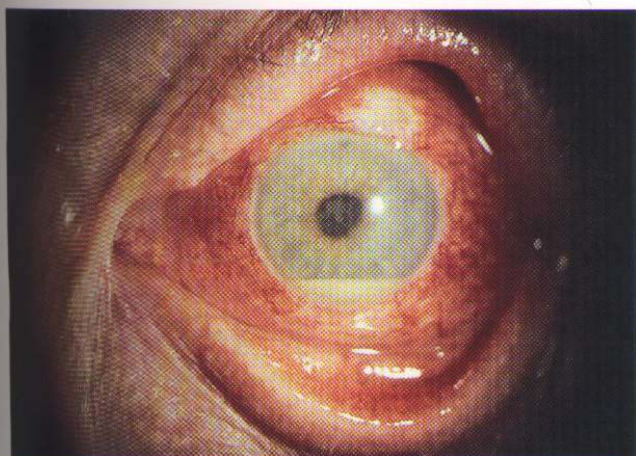


Fig. 9.171
Endophthalmitis with hypopyon following trabeculectomy

Bleb-associated endophthalmitis

1. **Presentation** is with a short history of rapidly worsening vision, pain and redness.
2. **Signs**
   - White milky bleb.
   - Severe anterior uveitis which may be associated with hypopyon (Fig. 9.171).
   - Vitritis and impairment of the red reflex.
3. **Treatment** involves vitreous biopsy and intravitreal antibiotics (*see* Chapter 8).

> NB: Successfully treated eyes remain at risk of recurrent infection.

Non-penetrating filtration surgery

In non-penetrating filtration surgery the anterior chamber is not entered, thus reducing the incidence of postoperative overfiltration and hypotony. In general, however, IOP reduction is inferior to that achieved by trabeculectomy; conventional filtration is therefore still the procedure of choice when the target IOP is in the lower teens. Non-penetrating surgery consists of fashioning two lamellar scleral flaps and excising the deep flap, leaving behind a thin membrane consisting of trabeculum/Descemet membrane through which aqueous diffuses from the anterior chamber to the subconjunctival space. The two currently used procedures are: (a) *deep sclerectomy*, in which bleb formation often occurs; and (b) *viscocanalostomy*, in which bleb formation is infrequent.

Deep sclerectomy

1. A fornix-based conjunctival flap is prepared.
2. A superficial partial-thickness scleral flap is dissected into clear cornea.
3. A second deeper partial-thickness scleral flap approximately 4 mm wide is dissected forward to the canal of Schlemm and is excised.
4. A collagen implant drainage device may be placed under the superficial scleral flap.
5. The superficial flap is loosely approximated and the conjunctival incision closed.

Viscocanalostomy

1. A fornix-based conjunctival flap is dissected.
2. A superficial partial-thickness flap is dissected to approximately one-third scleral thickness.
3. A second deeper scleral flap is dissected to provide access to Schlemm canal.
4. High-viscosity viscoelastic substance is injected into Schlemm canal with a special cannula.
5. A Descemet 'window' is created by gently dissecting the deep flap anterior to Schlemm canal and then excising it.
6. The superficial scleral flap is tightly sutured to minimize subconjunctival fluid flow and bleb formation.
7. Viscoelastic substance is injected into the area of the sclerotomy.
8. The conjunctiva is closed.

Adjunctive antimetabolites

Adjunctive antimetabolites inhibit the natural healing response that may preclude successful filtration surgery. They should, however, be used with caution because of the serious nature of potential complications, and primarily considered in the context of known risk factors for failure of trabeculectomy.

Indications

1. **High risk factors**
   - Neovascular glaucoma.
   - Previous failed trabeculectomy or artificial filtering devices.
   - Certain secondary glaucomas (e.g. inflammatory, post-traumatic angle recession and iridocorneal endothelial syndrome).
   - Chronic cicatrizing conjunctival inflammation.
2. **Intermediate risk factors**
   - Patients on topical antiglaucoma medication (particularly sympathomimetics) for over 3 years.
   - Previous conjunctival surgery.
   - Combined procedure for glaucoma and cataract.
3. **Low risk factors**
   - Black patients.
   - Patients under the age of 40 years.

> ***NB:*** In uncomplicated glaucoma the use of low-dose antimetabolites may improve long-term control of IOP but this benefit should be weighed against possible complications such as corneal epithelial defects, chronic hypotony and late-onset bleb leakage.

General precautions

- Antimetabolite therapy should be used with great caution when the conjunctiva has been recessed or where the limbal stem cell population is decreased (e.g. alkali burns, ocular pemphigoid).
- The filtration site should never be placed inferiorly because of the increased risk of late intraocular infection.
- The antimetabolite must not come into contact with the edges of the conjunctival incisions or the corneal endothelium.
- Tenon capsule and conjunctiva should be sutured separately in two layers, with a round-bodied needle.
- Patients should be advised of the potential late complications, in particular the high incidence of cystic bleb formation. They should also be made aware that additional surgery may be required in the event of late hypotony. Because of the potential for late bleb-related endophthalmitis they should be told of the risks associated with contact lens wear, swimming in a public pool and the danger of using contaminated drops.

5-Fluorouracil

5-Fluorouracil (5-FU) inhibits DNA synthesis and is active on the 'S' phase (synthesis phase) of the cell cycle. Fibroblastic proliferation is inhibited, but fibroblastic attachment and migration are unaffected. The technique is as follows:

1. A conjunctival flap is dissected.
2. A cellulose sponge measuring 4.5 × 4.5 mm is soaked in a 50 mg/ml solution of 5-FU.
3. The sponge is placed under the dissected flap of Tenon capsule at the site of filtration, making sure that the edges of the conjunctival incision are not exposed to the drug.
4. The sponge is removed after 5 minutes.
5. The space between the conjunctiva and episclera is thoroughly irrigated with balanced salt solution.
6. The trabeculectomy is completed.

Mitomycin C

Mitomycin C (MMC) is an alkylating agent rather than an antimetabolite which selectively inhibits DNA replication, mitosis and protein synthesis. The drug inhibits proliferation of fibroblasts, suppresses vascular ingrowth and *in vitro* has been shown to be much more potent than 5-FU. Optimum concentration and exposure time are not known and vary between 0.2–0.5 mg/ml and 1–5 minutes. In general, low or intermediate risk indicates use of a low concentration (0.2 mg/ml), while high risk implies the need for a higher concentration (0.4–0.5 mg/ml). Higher concentrations and extended exposure times are associated with an increased risk of complications. The technique of application is the same as for 5-FU and great care should be taken to prevent contamination of the anterior chamber.

Artificial drainage shunts

Artificial drainage shunts are plastic devices which create a communication between the anterior chamber and sub-Tenon space. All such shunts consist of a tube attached to a posterior episcleral explant. Some contain pressure-sensitive valves for regulation of aqueous flow. Because of the many postoperative complications associated with this type of surgery, drainage shunts should be installed only by surgeons thoroughly trained in their use.

Indications

- Uncontrolled glaucoma despite previous trabeculectomy with adjunctive antimetabolite therapy.
- Secondary glaucoma where routine trabeculectomy, with or without adjunctive antimetabolites, is unlikely to be successful. Examples include neovascular glaucoma, aniridia and glaucoma following traumatic anterior segment disruption.
- Severe conjunctival scarring precluding accurate dissection of the conjunctiva.
- Certain congenital glaucomas where conventional procedures have failed (i.e. goniotomy, trabeculotomy and trabeculectomy).

Implant types

The currently used implants are the Molteno (Fig. 9.172), Baerveldt, Krupin and Ahmed. They are based on a design

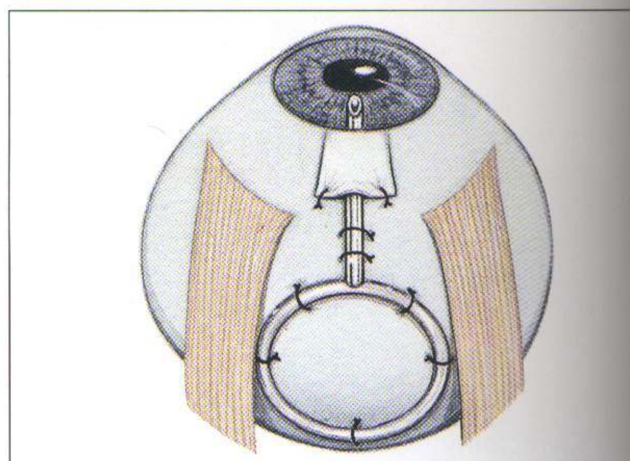


Fig. 9.172
Molteno implant

originally described by Molteno, which incorporates a scleral explant to promote the formation of a functioning bleb. An open tube, one end of which is placed in the anterior chamber, shunts aqueous humour into an encapsulated area around the explant located 10–12 mm posterior to the limbus. Reduction of IOP is due to passive, pressure-dependent flow of aqueous across the capsular wall. The magnitude of pressure reduction depends on the resistance to aqueous flow (the thicker the capsule, the higher the IOP) and the total surface area of encapsulation (the larger the surface, the lower the IOP).

Complications

1. **Excessive drainage** may occur due to leakage around or down the tube and result in a shallow anterior chamber (Fig. 9.173). Leakage down the tube may be minimized by the use of releasable or dissolvable sutures to occlude the tube during the early postoperative period.

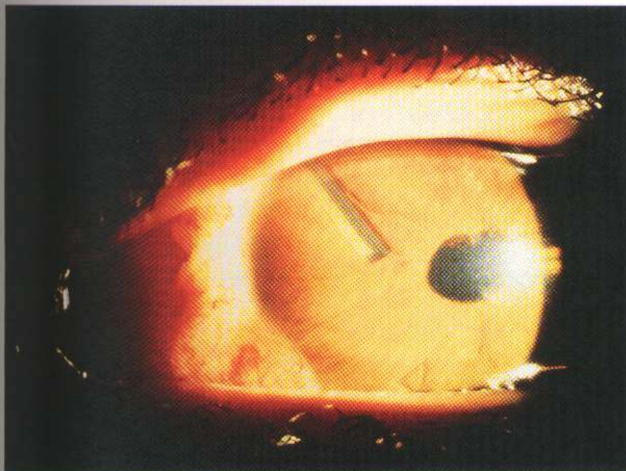


Fig. 9.173
Flat anterior chamber secondary to excessive drainage by an artificial shunt (Courtesy of J. Salmon)

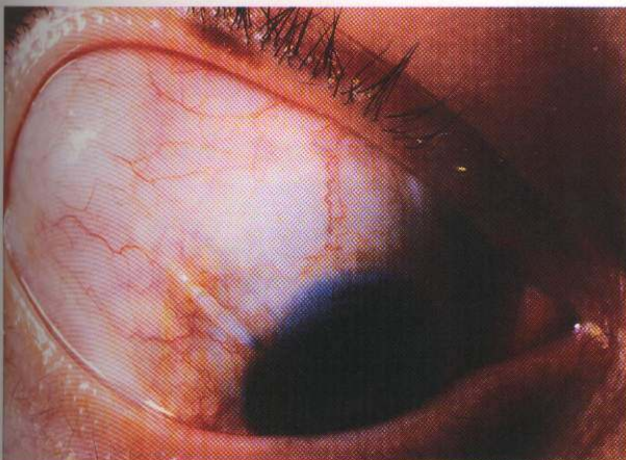


Fig. 9.174
Erosion of a drainage tube through the conjunctiva (Courtesy of J. Salmon)

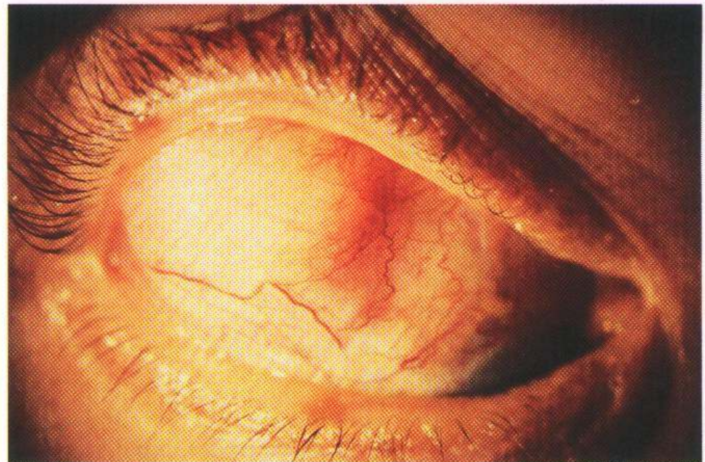


Fig. 9.175
Encapsulation of the bleb over the footplate (Courtesy of J. Salmon)

2. **Corneal decompensation** secondary to endothelial touch by a poorly positioned tube.
3. **Cataract** may develop if the end of the tube touches the lens.
4. **Tube retraction** from the anterior chamber is uncommon, but may occur if the tube has been cut too short.
5. **Tube erosion** through the conjunctiva (Fig. 9.174) can be avoided by placing a donor scleral flap between the tube and Tenon capsule.
6. **Drainage failure** may occur as a result of blockage of the end of the tube by vitreous, blood or iris tissue.
7. **Diplopia** due to muscle imbalance has been reported, particularly if the footplate passes under a muscle or if a device with a large drainage area has been used.
8. **Bleb encapsulation** over the footplate (Fig. 9.175) may result in poor drainage. This occurs in about 10% of cases and is the most significant late complication.
9. **Late endophthalmitis**.

Results

These depend on the type of glaucoma. An IOP < 21 mmHg is achieved in 50–70% of cases but topical medication is often required to maintain the IOP at this level. Less than 33% of cases achieve adequate control of IOP without additional medical therapy. The long-term success rate in neovascular glaucoma is particularly disappointing because of progressive retinal disease with loss of vision and late development of phthisis bulbi. Adjunctive mitomycin C may enhance the success rate of drainage shunt surgery.